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(54) Title: NUCLEOTIDE AND AMINO ACID SEOUENCES OF THE ENVELOPE 1 GENE OF 51 HEPATITIS C VIRUS ISOLATES AND THE USE OF REAGENTS DERIVED THEREFROM AS DIAGNOSTIC REAGENTS AND VACCINES

#### (57) Abstract

The nucleotide and deduced amino acid sequences of 51 cDNAs are disclosed where each cDNA encodes the envelope 1 gene of an isolate of hepatitis C virus (HCV). The invention relates to the oligonucleotides, peptides and recombinant envelope 1 proteins derived from these sequences and their use in diagnostic methods and vaccines.

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#### Title of the Invention

NUCLEOTIDE AND AMINO ACID SEQUENCES OF THE ENVELOPE 1 GENE OF 51 HEPATITIS C VIRUS ISOLATES AND THE USE OF REAGENTS DERIVED THEREFROM AS DIAGNOSTIC REAGENTS AND VACCINES

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#### Field Of Invention

The present invention is in the field of hepatitis virology. The invention relates to the complete nucleotide and deduced amino acid sequences of the envelope 1 (E1) gene of 51 hepatitis C virus (HCV) isolates from around the world and the grouping of these isolates into twelve distinct HCV genotypes. More specifically, this invention relates to oligonucleotides, peptides and recombinant proteins derived from the envelope 1 gene sequences of the 51 isolates of hepatitis C virus and to diagnostic methods and vaccines which employ these reagents.

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#### Background Of Invention

Hepatitis C, originally called non-A, non-B hepatitis, was first described in 1975 as a disease serologically distinct from hepatitis A and hepatitis B (Feinstone, S.M. et al. (1975) N. Engl. J. Med. 292:767-770). Although hepatitis C was (and is) the leading type of transfusion-associated hepatitis as well as an important part of community-acquired hepatitis, little progress was made in understanding the disease until the recent identification of hepatitis C virus (HCV) as the causative agent of hepatitis C via the cloning and sequencing of the HCV genome (Choo, A.L. et al. (1989) Science 288:359-362). The sequence information generated by this study resulted in the characterization of HCV as a small, enveloped, positive-stranded RNA virus and led to the demonstration that HCV is a major cause of both acute and chronic hepatitis worldwide (Weiner, A.J. et al. (1990) Lancet

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vaccines.

335:1-3). These observations, combined with studies showing that over 50% of acute cases of hepatitis C progress to chronicity with 20% of these resulting in cirrhosis and an undetermined proportion progressing to liver cancer, have led to tremendous efforts by investigators within the hepatitis C field to develop diagnostic assays and vaccines which can detect and prevent

hepatitis C infection.

The cloning and sequencing of the HCV genome by Choo et al. (1989) has permitted the development of serologic tests which can detect HCV or antibody to HCV (Kuo, G. et al. (1989) Science 244:362-364). In addition, the work of Choo et al. has also allowed the development of methods for detecting HCV infection via amplification of HCV RNA sequences by reverse transcription and cDNA polymerase chain reaction (RT-PCR) using primers derived from the HCV genomic sequence (Weiner, A.J. et al.). However, although the development of these diagnostic methods has resulted in improved diagnosis of HCV infection, only approximately 60% of cases of hepatitis C are associated with a factor identified as contributing to transmission of HCV (Alter, M.J. et al. (1989) JAMA 262:1201-1205). This observation suggests that effective control of hepatitis C transmission is likely to occur only via universal pediatric vaccination as has been initiated recently for hepatitis B virus. Unfortunately, attempts to date to protect chimpanzees from hepatitis C infection via administration of recombinant vaccines have had only limited success. Moreover, the apparent genetic heterogeneity of HCV, as indicated by the recent assignment of all available HCV isolates to one of four genotypes, I-IV (Okamoto, H. et al. (1992) J. Gen. Virol; 73:673-679), presents additional hurdles which must be overcome in order to develop accurate and effective diagnostic assays and

For example, one possible obstacle to the

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development of effective hepatitis C vaccines would arise if the observed genetic heterogeneity of HCV reflects serologic heterogeneity. In such a case, the most genetically diverse strains of HCV may then represent different serotypes of HCV with the result being that 5 infection with one strain may not protect against infection with another. Indeed, the inability of one strain to protect against infection with another strain was recently noted by both Farci et al. (Farci, P. et al. (1992) Science 258:135-140) and Prince et al. (Prince, A.M. et al. (1992) 10 J. Infect. Dis. 165:438-443), each of whom presented evidence that while infection with one strain of HCV does modify the degree of the hepatitis C associated with the reinfection, it does not protect against reinfection with a closely related strain. The genetic heterogeneity among 15 different HCV strains also increases the difficulty encountered in developing RT-PCR assays to detect HCV infection since such heterogeneity often results in falsenegative results because of primer and template mismatch. In addition, currently used serologic tests for detection 20 of HCV or for detection of antibody to HCV are not sufficiently well developed to detect all of the HCV genotypes which might exist in a given blood sample. Finally, in terms of choosing the proper treatment modality to combat hepatitis infection, the inability of presently 25 available serologic assays to distinguish among the various genotypes of HCV represents a significant shortcoming in that recent reports suggest that an HCV-infected patient's response to therapy might be related to the genotype of the infectious virus (Yoshioka, K. et al. (1992) Hepatology 16:293-299; Kanai, K. et al. (1992) Lancet 339:1543; Lan, 30 J.Y.N. et al. (1992) Hepatology 16:209A). Indeed, the data presented in the above studies suggest that the closely related genotypes I and II are less responsive to interferon therapy than are the closely related genotypes

III and IV. Moreover, preliminary data by Pozzato et al.

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(Pozzato, G. et al. (1991) Lancet 338:509) suggests that different genotypes may be associated with different types or degrees of clinical disease. Taken together, these studies suggest that before effective vaccines against HCV infection can be developed, and indeed, before more accurate and effective methods for diagnosis and treatment of HCV infection can be produced, one must obtain a greater knowledge about the genetic and serologic diversity of HCV isolates.

In a recent attempt to gain an understanding of 10 the extent of genetic heterogeneity among HCV strains, Bukh et al. carried out a detailed analysis of HCV isolates via the use of PCR technology to amplify different regions of the HCV genome (Bukh, J. et al. (1992a) Proc. Natl. Acad. Sci. 89:187-191). Following PCR amplification, the 5'noncoding (5' NC) portion of the genomes of various HCV 15 isolates were sequenced and it was found that primer pairs designed from conserved regions of the 5' NC region of the HCV genome were more sensitive for detecting the presence of HCV than were primer pairs representing other portions 20 of the genome (Bukh, J. et al. (1992b) Proc. Natl. Acad. Sci. U.S.A. 89:4942-4946). In addition, the authors noted that although many of the HCV isolates examined could be classified into the four genotypes described by Okamoto et al. (1992), other previously undescribed genotypes emerged based on genetic heterogeneity observed in the 5' NC region 25 of the various isolates. One of the most prominent of these newly noted genotypes comprised a group of related viruses that contained the most genetically divergent 5' NC regions of those studied. This group of viruses, tentatively classified as a fifth genotype, are very 30 similar to strains recently described by others (Cha, T.-A et al. (1992) Proc. Natl. Acad. Sci. U.S.A. 89:7144-7148; Chan, S-W. et al. (1992) J. Gen. Virol., 73:1131-1141 and Lee, C-H et al. (1992) J. Clin. Microbio. 30:1602-1604).

In addition, at least four more putative genotypes were

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identified thereby providing evidence that the genetic heterogeneity of HCV was more extensive than previously appreciated.

However, while the studies of Bukh et al. (1992a and b) provided new and useful information on the genetic heterogeneity of HCV, it is widely appreciated by those skilled in the art that the three structural genes of HCV, core (C), envelope (E1) and envelope 2/nonstructural 1 (E2/NS1) are the most important for the development of serologic diagnostics and vaccines since it is the product of these genes that constitutes the hepatitis C virion. Thus, a determination of the nucleotide sequence of one or all of the structural genes of a variety of HCV isolates would be useful in designing reagents for use in diagnostic assays and vaccines since a demonstration of genetic heterogeneity in a structural gene(s) of HCV isolates might suggest that some of the HCV genotypes represent distinct serotypes of HCV based upon the previously observed relationship between genetic heterogeneity and serologic heterogeneity among another group of single-stranded, positive-sense RNA viruses, the picornaviruses (Ruechert, R.R. "Picornaviridae and their replication", in Fields, B.N. et al., eds. Virology, New York: Raven Press, Ltd. (1990) 507-548).

### 25 <u>Summary of Invention</u>

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The present invention relates to 51 cDNAs, each encoding the complete nucleotide sequence of the envelope 1 (E1) gene of an isolate of human hepatitis C virus (HCV).

The present invention also relates to the nucleic acid and deduced amino acid sequences of these E1 cDNAs.

It is an object of this invention to provide synthetic nucleic acid sequences capable of directing production of recombinant E1 proteins, as well as equivalent natural nucleic acid sequences. Such natural nucleic acid sequences may be isolated from a cDNA or

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genomic library from which the gene capable of directing synthesis of the R1 proteins may be identified and isolated. For purposes of this application, nucleic acid sequence refers to RNA, DNA, cDNA or any synthetic variant thereof which encodes for peptides.

The invention also relates to the method of preparing recombinant E1 proteins derived from the E1 cDNA sequences by cloning the nucleic acid and inserting the cDNA into an expression vector and expressing the recombinant protein in a host cell.

The invention also relates to isolated and substantially purified recombinant E1 proteins and analogs thereof encoded by the E1 cDNAs.

The invention further relates to the use of recombinant E1 proteins as diagnostic agents and as vaccines.

The invention also relates to the use of singlestranded antisense poly- or oligonucleotides derived from the E1 cDNAs to inhibit the expression of the hepatitis C E1 gene.

The invention further relates to multiple computer-generated alignments of the nucleotide and deduced amino acid sequences of the 51 E1 cDNAs. These multiple sequence alignments serve to highlight regions of homology and non-homology between different sequences and hence, can be used by one skilled in the art to design peptides and oligonucleotides useful as reagents in diagnostic assays and vaccines.

The invention therefore also relates to purified and isolated peptides and analogs thereof derived from E1 cDNA sequences.

The invention further relates to the use of these peptides as diagnostic agents and vaccines.

The present invention also encompasses methods of detecting antibodies specific for hepatitis C virus in biological samples. The methods of detecting HCV or

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antibodies to HCV disclosed in the present invention are useful for diagnosis of infection and disease caused by HCV and for monitoring the progression of such disease. Such methods are also useful for monitoring the efficacy of therapeutic agents during the course of treatment of HCV infection and disease in a mammal.

The invention also provides a kit for the detection of antibodies specific for HCV in a biological sample where said kit contains at least one purified and isolated peptide derived from the E1 cDNA sequences.

The invention further provides isolated and purified genotype-specific oligonucleotides and analogs thereof derived from El cDNA sequences.

The invention also relates to a method for detecting the presence of hepatitis C virus in a mammal, said method comprising analyzing the RNA of a mammal for the presence of hepatitis C virus. The invention further relates to a method for determining the genotype of hepatitis C virus present in a mammal. This method is useful in determining the proper course of treatment for an HCV-infected patient.

The invention also provides a diagnostic kit for the detection of hepatitis C virus in a biological sample. The kit comprises purified and isolated nucleic acid sequences useful as primers for reverse-transcription polymerase chain reaction (RT-PCR) analysis of RNA for the presence of hepatitis C virus.

The invention further provides a diagnostic kit for the determination of the genotype of a hepatitis C virus present in a mammal. The kit comprises purified and isolated nucleic acid sequences useful as primers for RT-PCR analysis of RNA for the presence of HCV in a biological sample and purified and isolated nucleic acid sequences useful as hybridization probes in determining the genotype of the HCV isolate detected in PCR.

This invention also relates to pharmaceutical

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compositions for use in prevention or treatment of hepatitis C in a mammal.

### Description of Figures

Figures 1 A-H show computer generated sequence 5 alignments of the nucleotide sequences of the 51 HCV E1 cDNAs. The single letter abbreviations used for the nucleotides shown in Figures 1A-H are those standardly used Figure 1A shows the alignment of SEQ ID NOs:1-8 to produce a consensus sequence for genotype I/la. 10 Figure 1B shows the alignment of SEQ ID NOs:9-25 to produce a consensus sequence for genotype II/lb. Figure 1C shows the alignment of SEQ ID NOs:26-29 to produce a consensus sequence for genotype III/2a. Figure 1D shows the alignment of SEQ ID NOs:30-33 to produce a consensus 15 sequence for genotype IV/2b. Figure 1E shows the alignment of SEQ ID NOs:35-39 to produce a consensus sequence for genotype V/3a. Figure 1F shows the computer alignment of SEQ ID NOs:42-43 to produce a consensus sequence for genotype 4C. Figure 1G shows the alignment of SEQ ID 20 NOs:45-50 to produce a consensus sequence for genotype 5a. The nucleotides shown in capital letters in the consensus sequences of Figures 1A-G are those conserved within a genotype while nucleotides shown in lower case letters in the consensus sequences are those variable within a 25 genotype. In addition, in Figures 1A-E and 1G, when the lower case letter is shown in a consensus sequence, the lower case letter represents the nucleotide found most frequently in the sequences aligned to produce the consensus sequence. In Figure 1E, the lower case letters 30 shown in the consensus sequence are nucleotides in SEQ ID NO:42 which differ from nucleotides found in the same positions in SEQ ID NO:43. Finally, a hyphen at a nucleotide position in the consensus sequences in Figures 1A-6 indicates that two nucleotides were found in equal

numbers at that position in the aligned sequences.

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aligned sequences, nucleotides are shown in lower case
letters if they differed from the nucleotides of both
adjacent isolates. Figure 1H shows the alignment of the
consensus sequences of Figures 1A-G with SEQ ID NO:34
(genotype 2c), SEQ ID NO:40 (genotype 4a), SEQ ID NO:41

(genotype 4b), SEQ ID NO:44 (genotype 4d) and SEQ ID NO:51
(genotype 6a) to produce a consensus sequence for all
twelve genotypes. This consensus sequence is shown as the
bottom line of Figure 1H where the nucleotides shown in
capital letters are conserved among all genotypes and a

blank space indicates that the nucleotide at that position
is not conserved among all genotypes.

Figures 2A-H show computer alignments of the deduced amino acid sequences of the 51 HCV E1 cDNAs. single letter abbreviations used for the amino acids shown 15 in Figures 2A-H follow the conventional amino acid shorthand for the twenty naturally occurring amino acids. Figure 2A shows the alignment of SEQ ID NOs:52-59 to produce a consensus sequence for genotype I/la. Figure 2B shows the alignment of SEQ ID NOs:60-76 to produce a 20 consensus sequence for genotype II/1b. Figure 2C shows the alignment of SEQ ID NOs:77-80 to produce a consensus sequence for genotype III/2a. Figure 2D shows the alignment of SEQ ID NOs:81-84 to produce a consensus sequence for genotype IV/2b. Figure 2E shows the alignment 25 of SEQ ID NOs:86-90 to produce a consensus sequence for genotype V/3a. Figure 2F shows the computer alignment of SEQ ID NOs:93-94 to produce a consensus sequence for genotype 4c. Figure 2G shows the alignment of SEO ID NOs:96-101 to produce a consensus sequence for genotype 5a. The amino acids shown in capital letters in the consensus 30 sequences of Figures 2A-G are those conserved within a genotype while amino acids shown in lower case letters in the consensus sequences are those variable within a genotype. In addition, in Figures 2A-E and 2G when the 35 lower case letter is shown in a consensus sequence, the

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letter represents the amino acid found most frequently in the sequences aligned to produce the consensus sequence. In Figure 2E, the lower case letters shown in the consensus sequence are amino acids in SEQ ID NO:93 which differ from amino acids found in the same positions in SEQ ID NO:94.

5 Finally, a hyphen at an amino acid position in the consensus sequences of Figures 2A-G indicates that two amino acids were found in equal numbers at that position in the aligned sequences. In the aligned sequences, amino acids are shown in lower case letters if they differed from 10 the amino acids of both adjacent isolates. Figure 2H shows the alignment of the consensus sequences of Figures 1A-G with SEQ ID NO:85 (genotype 2c), SEQ ID NO:91 (genotype 4a), SEQ ID NO:92 (genotype 4b), SEQ ID NO:95 (genotype 4d) and SEQ ID NO:102 (genotype 6a) to produce a consensus 15 sequence for all twelve genotypes. This consensus sequence is shown as the bottom line of Figure 2H where the amino acids shown in capital letters are conserved among all genotypes and a blank space indicates that the amino acid

at that position is not conserved among all genotypes.

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Figure 3 shows multiple sequence alignment of the deduced amino acid sequence of the E1 gene of 51 HCV isolates collected worldwide. The consensus sequence of the E1 protein is shown in boldface (top). consensus sequence cysteine residues are highlighted with stars, potential N-linked glycosylation sites are underlined, and invariant amino acids are capitalized, whereas variable amino acids are shown in lower case letters. In the alignment, amino acids are shown in lower case letters if they differed from the amino acid of both adjacent isolates. Amino acid residues shown in bold print in the alignment represent residues which at that position in the amino acid sequence are genotype-specific. acids that were invariant among all HCV isolates are shown as hyphens (-) in the alignment. Amino acid positions correspond to those of the HCV prototype sequence (HCV-1,

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Choo, L. et al. (1991) Proc. Natl. Acad. Sci. USA 88:2451-2455) with the first amino acid of the E1 protein at position 192. The grouping of isolates into 12 genotypes (I/la, II/lb, III/2a, IV/2b, V/3a, 2c, 4a, 4b, 4c, 4d, 5a and 6a) is indicated.

Figure 4 shows a dendrogram of the genetic relatedness of the twelve genotypes of HCV based on the percent amino acid identity of the E1 gene of the HCV genome. The twelve genotypes shown are designated as I/1a, II/1b, III/2a, IV/2b, V/3a, 2c, 4a, 4b, 4c, 4d, 5a and 6a.

The shaded bars represent a range showing the maximum and minimum homology between the amino acid sequence of any one isolate of the genotype indicated and the amino acid sequence of any other isolate.

Figure 5 shows the distribution of the complete 15 E1 gene sequence of 74 HCV isolates into the twelve HCV genotypes in the 12 countries studied. For 51 of these HCV isolates, including 8 isolates of genotype I/la, 17 isolates of genotype II/lb and 26 isolates comprising the additional 10 genotypes, the complete E1 gene sequence was 20 determined. In the remaining 23 isolates, all of genotypes I/la and II/lb, the genotype assignment was based on only a partial E1 gene sequence. The partially sequenced isolates did not represent additional genotypes in any of the 12 countries. The number of isolates of a particular genotype 25 is given in each of the 12 countries studied. For ease of viewing, those genotypes designated by two terms (e.g., I/la) are indicated by the latter term (e.g. 1a). designations used for each country are: Denmark (DK); Dominican Republic (DR); Germany (D); Hong Kong (HK); India 30 (IND); Sardinia, Italy (S); Peru (P); South Africa (SA); Sweden (SW); Taiwan (T); United States (US); and Zaire (Z). National borders depicted in this figure represent those existing at the time of sampling.

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# Detailed Description Of Invention

The present invention relates to 51 cDNAs, each encoding the complete nucleotide sequence of the envelope 1 (E1) gene of an isolate of human hepatitis C virus (HCV). The cDNAs of the present invention were obtained as follows. Viral RNA was extracted from serum collected from humans infected with hepatitis C virus and the viral RNA was then reverse transcribed and amplified by polymerase chain reaction using primers deduced from the sequence of the HCV strain H-77 (Ogata, N. et al. (1991) Proc. Natl.

10 Acad. Sci. U.S.A. 88:3392-3396). The amplified cDNA was then isolated by gel electrophoresis and sequenced.

The present invention further relates to the nucleotide sequences of the cDNAs encoding the E1 gene of the 51 HCV isolates. These nucleotide sequences are shown in the sequence listing as SEQ ID NO:1 through SEQ ID NO:51.

The abbreviations used for the nucleotides are those standardly used in the art.

The deduced amino acid sequence of each of SEQ ID NO:1 through SEQ ID NO:51 are presented in the sequence listing as SEQ ID NO:52 through SEQ ID NO:102 where the amino acid sequence in SEQ ID NO:52 is deduced from the nucleotide sequence shown in SEQ ID NO:1, the amino acid sequence shown in SEQ ID NO:53 is deduced from the nucleotide sequence shown in SEQ ID NO:2 and so on. The deduced amino acid sequence of each of SEQ ID Nos:52-102 starts at nucleotide 1 of the corresponding sequence shown in SEQ ID NOs:1-51 and extends 595 nucleotides.

The three letter abbreviations used in SEQ ID Nos:52-102 follow the conventional amino acid shorthand for the twenty naturally occurring amino acids.

Preferably, the E1 proteins or peptides of the present invention are substantially homologous to, and most preferably biologically equivalent to, the native HCV E1 proteins or peptides. By "biologically equivalent" as used

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throughout the specification and claims, it is meant that the compositions are immunogenically equivalent to the native E1 proteins or peptides. The E1 proteins or peptides of the present invention may also stimulate the production of protective antibodies upon injection into a 5 mammal that would serve to protect the mammal upon challenge with HCV. By "substantially homologous" as used throughout the ensuing specification and claims to describe El proteins and peptides, it is meant a degree of homology in the amino acid sequence to the native E1 proteins or 10 peptides. Preferably the degree of homology is in excess of 90, preferably in excess of 95, with a particularly preferred group of proteins being in excess of 99 homologous with the native El proteins or peptides.

Variations are contemplated in the cDNA sequences shown in SEQ ID NO:1 through SEQ ID NO:51 which will result in a DNA sequence that is capable of directing production of analogs of the corresponding envelope 1 (E1) protein shown in SEQ ID NO:52 through SEQ ID NO:102. It should be noted that the DNA sequences set forth above represent a preferred embodiment of the present invention. Due to the degeneracy of the genetic code, it is to be understood that numerous choices of nucleotides may be made that will lead to a DNA sequence capable of directing production of the instant E1 protein or its analogs. As such, DNA sequences which are functionally equivalent to the sequence set forth above or which are functionally equivalent to sequences that would direct production of analogs of the E1 proteins produced pursuant to the amino acid sequences set forth above, are intended to be encompassed within the present invention.

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The term analog as used throughout the specification or claims to describe the E1 proteins or peptides of the present invention, includes any protein or peptide having an amino acid residue sequence substantially identical to a sequence specifically shown herein in which

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one or more residues have been conservatively substituted with a biologically equivalent residue. Examples of conservative substitutions include the substitution of one-polar (hydrophobic) residue such as isoleucine, valine, leucine or methionine for another, the substitution of one polar (hydrophilic) residue for another such as between arginine and lysine, between glutamine and asparagine, between glycine and serine, the substitution of one basic residue such as lysine, arginine or histidine for another, or the substitution of one acidic residue, such as aspartic acid or glutamic acid for another.

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The phrase "conservative substitution" also includes the use of a chemically derivatized residue in place of a non-derivatized residue provided that the resulting protein or peptide is biologically equivalent to the native E1 protein or peptide.

"Chemical derivative" refers to an El protein or peptide having one or more residues chemically derivatized by reaction of a functional side group. Examples of such derivatized molecules, include but are not limited to, those molecules in which free amino groups have been derivatized to form amine hydrochlorides, p-toluene sulfonyl groups, carbobenzoxy groups, t-butyloxycarbonyl groups, chloracetyl groups or formyl groups. Free carboxyl groups may be derivatized to form salts, methyl and ethyl esters or other types of esters or hydrazides. hydroxyl groups may be derivatized to form O-acyl or Oalkyl derivatives. The imidazole nitrogen of histidine may be derivatized to form N-imbenzylhistidine. Also included as chemical derivatives are those proteins or peptides which contain one or more naturally-occurring amino acid derivatives of the twenty standard amino acids. For examples: 4-hydroxyproline may be substituted for proline; 5-hydroxylysine may be substituted for lysine; 3methylhistidine may be substituted for histidine; homoserine may be substituted for serine; and ornithine may

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be substituted for lysine. The E1 protein or peptide of the present invention also includes any protein or peptide having one or more additions and/or deletions or residues relative to the sequence of a peptide whose sequence is shown herein, so long as the peptide is biologically equivalent to the native E1 protein or peptide.

The present invention also includes a recombinant DNA method for the manufacture of HCV E1 proteins. In this method, natural or synthetic nucleic acid sequences may be used to direct the production of E1 proteins.

In one embodiment of the invention, the method comprises:

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- (a) preparation of a nucleic acid sequence capable of directing a host organism to produce HCV El protein;
- 15 (b) cloning the nucleic acid sequence into a vector capable of being transferred into and replicated in a host organism, such vector containing operational elements for the nucleic acid sequence;
- (c) transferring the vector containing the nucleic acid and operational elements into a host organism capable of expressing the protein;
  - (d) culturing the host organism under conditions appropriate for amplification of the vector and expression of the protein; and
    - (e) harvesting the protein.

In another embodiment of the invention, the method for the recombinant DNA synthesis of an HCV E1 protein encoded by any one of the nucleic acid sequences shown in SEQ ID NOs:1-51 comprises:

(a) culturing a transformed or transfected host organism containing a nucleic acid sequence capable of directing the host organism to produce a protein, under conditions such that the protein is produced, said protein exhibiting substantial homology to a native E1 protein isolated from HCV having the amino acid sequence according

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to any one of the amino acid sequences shown in SEQ ID NOs:52-102 or combinations thereof.

In one embodiment, the RNA sequence of an HCV isolate was isolated and cloned to cDNA as follows. Viral RNA is extracted from a biological sample collected from human subjects infected with hepatitis C and the viral RNA is then reverse transcribed and amplified by polymerase chain reaction using primers deduced from the sequence of HCV strain H-77 (Ogata et al. (1991)). Preferred primer sequences are shown as SEQ ID NOs:103-108 in the sequence listing. Once amplified, the PCR fragments are isolated by gel electrophoresis and sequenced.

The vectors contemplated for use in the present invention include any vectors into which a nucleic acid sequence as described above can be inserted, along with any preferred or required operational elements, and which vector can then be subsequently transferred into a host organism and replicated in such organisms. Preferred vectors are those whose restriction sites have been well documented and which contain the operational elements preferred or required for transcription of the nucleic acid sequence.

The "operational elements" as discussed herein include at least one promoter, at least one operator, at least one leader sequence, at least one terminator codon, and any other DNA sequences necessary or preferred for appropriate transcription and subsequent translation of the vector nucleic acid. In particular, it is contemplated that such vectors will contain at least one origin of replication recognized by the host organism along with at least one selectable markers and at least one promoter sequence capable of initiating transcription of the nucleic acid sequence.

In construction of the recombinant for expression cloning vector of the present invention, it should additionally be noted that multiple copies of the nucleic

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acid sequence and its attendant operational elements may be inserted into each vector. In such an embodiment, the host organism would produce greater amounts per vector of the desired El protein. The number of multiple copies of the DNA sequence which may be inserted into the vector is limited only by the ability of the resultant vector due to its size, to be transferred into and replicated and transcribed in an appropriate host microorganism.

In another embodiment, restriction digest fragments containing a coding sequence for E1 proteins can be inserted into a suitable expression vector that functions in prokaryotic or eukaryotic cells. By suitable is meant that the vector is capable of carrying and expressing a complete nucleic acid sequence coding for E1 protein. Preferred expression vectors are those that function in a eukaryotic cell. Examples of such vectors include but are not limited to vaccinia virus vectors, adenovirus or herpes viruses. A preferred vector is the baculovirus transfer vector, pBlueBac.

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In yet another embodiment, the selected recombinant expression vector may then be transfected into a suitable eukaryotic cell system for purposes of expressing the recombinant protein. Such eukaryotic cell systems include but are not limited to cell lines such as HeLa, MRC-5 or Cv-1. A preferred eukaryotic cell system is SF9 insect cells.

The expressed recombinant protein may be detected by methods known in the art including, but not limited to, Coomassie blue staining and Western blotting.

The present invention also relates to substantially purified and isolated recombinant El proteins. In one embodiment, the recombinant protein expressed by the SF9 cells can be obtained as a crude lysate or it can be purified by standard protein purification procedures known in the art which may include differential precipitation, molecular sieve chromatography,

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ion-exchange chromatography, isoelectric focusing, gel electrophoresis and affinity and immunoaffinity chromatography. The recombinant protein may be purified by passage through a column containing a resin which has bound thereto antibodies specific for the open reading frame (ORF) protein.

The present invention further relates to the use of recombinant E1 proteins as diagnostic agents and vaccines. In one embodiment, the expressed recombinant proteins of this invention can be used in immunoassays for diagnosing or prognosing hepatitis C in a mammal. For the purposes of the present invention, "mammal" as used throughout the specification and claims, includes, but is not limited to humans, chimpanzees, other primates and the like. In a preferred embodiment, the immunoassay is useful in diagnosing hepatitis C infection in humans.

Immunoassays of the present invention may be a radioimmunoassay, Western blot assay, immunofluorescent assay, enzyme immunoassay, chemiluminescent assay, immunohistochemical assay and the like. Standard techniques known in the art for ELISA are described in Methods in Immunodiagnosis, 2nd Edition, Rose and Bigazzi, eds., John Wiley and Sons, 1980 and Campbell et al., Methods of Immunology, W.A. Benjamin, Inc., 1964, both of which are incorporated herein by reference. Such assays may be a direct, indirect, competitive, or noncompetitive immunoassay as described in the art (Oellerich, M. 1984. J. Clin. Chem. Clin. BioChem 22:895-904) Biological samples appropriate for such detection assays include, but are not limited to serum, liver, saliva, lymphocytes or other mononuclear cells.

In a preferred embodiment, test serum is reacted with a solid phase reagent having surface-bound recombinant HCV E1 protein as an antigen. The solid surface reagent can be prepared by known techniques for attaching protein to solid support material. These attachment methods

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include non-specific adsorption of the protein to the support or covalent attachment of the protein to a reactive group on the support. After reaction of the antigen with anti-HCV antibody, unbound serum components are removed by washing and the antigen-antibody complex is reacted with a secondary antibody such as labelled anti-human antibody. The label may be an enzyme which is detected by incubating the solid support in the presence of a suitable fluorimetric or calorimetric reagent. Other detectable labels may also be used, such as radiolabels or colloidal gold, and the like.

The HCV E1 protein and analogs thereof may be prepared in the form of a kit, alone, or in combinations with other reagents such as secondary antibodies, for use in immunoassays.

In yet another embodiment the recombinant E1
proteins or analogs thereof can be used as a vaccine to
protect mammals against challenge with Hepatitis C. The
vaccine, which acts as an immunogen, may be a cell, cell
lysate from cells transfected with a recombinant expression
vector or a culture supernatant containing the expressed
protein. Alternatively, the immunogen is a partially or
substantially purified recombinant protein.

While it is possible for the immunogen to be administered in a pure or substantially pure form, it is preferable to present it as a pharmaceutical composition, formulation or preparation.

The formulations of the present invention, both for veterinary and for human use, comprise an immunogen as described above, together with one or more pharmaceutically acceptable carriers and optionally other therapeutic ingredients. The carrier(s) must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not deleterious to the recipient thereof. The formulations may conveniently be presented in unit dosage form and may be prepared by any method well-known in

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the pharmaceutical art.

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All methods include the step of bringing into association the active ingredient with the carrier which constitutes one or more accessory ingredients. In general, the formulations are prepared by uniformly and intimately bringing into association the active ingredient with liquid carriers or finely divided solid carriers or both, and then, if necessary, shaping the product into the desired formulation.

Formulations suitable for intravenous 10 intramuscular, subcutaneous, or intraperitoneal administration conveniently comprise sterile aqueous solutions of the active ingredient with solutions which are preferably isotonic with the blood of the recipient. formulations may be conveniently prepared by dissolving the 15 solid active ingredient in water containing physiologically compatible substances such as sodium chloride (e.g. 0.1-2.0m), glycine, and the like, and having a buffered pH compatible with physiological conditions to produce an aqueous solution, and rendering said solution sterile. 20 These may be present in unit or multi-dose containers, for example, sealed ampoules or vials.

The formulations of the present invention may incorporate a stabilizer. Illustrative stabilizers are preferably incorporated in an amount of 0.11-10,000 parts by weight per part by weight of immunogens. If two or more stabilizers are to be used, their total amount is preferably within the range specified above. These stabilizers are used in aqueous solutions at the appropriate concentration and pH. The specific osmotic pressure of such aqueous solutions is generally in the range of 0.1-3.0 osmoles, preferably in the range of 0.8-1.2. The pH of the aqueous solution is adjusted to be within the range of 5.0-9.0, preferably within the range of 6-8. In formulating the immunogen of the present invention, anti-adsorption agent may be used.

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Additional pharmaceutical methods may be employed to control the duration of action. Controlled release preparations may be achieved through the use of polymer to complex or adsorb the proteins or their derivatives. controlled delivery may be exercised by selecting 5 appropriate macromolecules (for example polyester, polyamino acids, polyvinyl pyrrolidone, ethylenevinylacetate, methylcellulose, carboxymethylcellulose, or protamine sulfate) and the concentration of macromolecules as well as the methods of 10 incorporation in order to control release. Another possible method to control the duration of action by controlled-release preparations is to incorporate the proteins, protein analogs or their functional derivatives, into particles of a polymeric material such as polyesters, 15 polyamino acids, hydrogels, poly(lactic acid) or ethylene vinylacetate copolymers. Alternatively, instead of incorporating these agents into polymeric particles, it is possible to entrap these materials in microcapsules prepared, for example, by coacervation techniques or by 20 interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly (methylmethacylate) microcapsules, respectively, or in colloidal drug delivery systems, for example, liposomes, albumin microspheres, microemulsions, nanoparticles, and nanocapsules or in macroemulsions. 25

When oral preparations are desired, the compositions may be combined with typical carriers, such as lactose, sucrose, starch, talc, magnesium stearate, crystalline cellulose, methyl cellulose, carboxymethyl cellulose, glycerin, sodium alginate or gum arabic among others.

The proteins of the present invention may be supplied in the form of a kit, alone, or in the form of a pharmaceutical composition as described above.

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Vaccination can be conducted by conventional

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methods. For example, the immunogen or immunogens (i.e. the E1 protein may be administered alone or in combination with the E1 proteins derived from other isolates of HCV) can be used in a suitable diluent such as saline or water, or complete or incomplete adjuvants. Further, the immunogen(s) may or may not be bound to a carrier to make

or complete or incomplete adjuvants. Further, the

immunogen(s) may or may not be bound to a carrier to make
the protein(s) immunogenic. Examples of such carrier
molecules include but are not limited to bovine serum
albumin (BSA), keyhole limpet hemocyanin (KLH), tetanus
toxoid, and the like. The immunogen(s) can be administered
by any route appropriate for antibody production such as
intravenous, intraperitoneal, intramuscular, subcutaneous,
and the like. The immunogen(s) may be administered once or
at periodic intervals until a significant titer of anti-HCV

The antibody may be detected in the

antibody is produced. The serum using an immunoassay.

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The administration of the immunogen(s) of the present invention may be for either a prophylactic or therapeutic purpose. When provided prophylactically, the immunogen(s) is provided in advance of any exposure to HCV or in advance of any symptom of any symptoms due to HCV infection. The prophylactic administration of the immunogen serves to prevent or attenuate any subsequent infection of HCV in a mammal. When provided therapeutically, the immunogen(s) is provided at (or shortly after) the onset of the infection or at the onset of any symptom of infection or disease caused by HCV. The therapeutic administration of the immunogen(s) serves to attenuate the infection or disease.

In addition to use as a vaccine, the compositions can be used to prepare antibodies to HCV El proteins. The antibodies can be used directly as antiviral agents. To prepare antibodies, a host animal is immunized using the El proteins native to the virus particle bound to a carrier as described above for vaccines. The host serum or plasma is collected following an appropriate time interval to provide

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a composition comprising antibodies reactive with the E1 protein of the virus particle. The gamma globulin fraction or the IgG antibodies can be obtained, for example, by use of saturated ammonium sulfate or DEAE Sephadex, or other techniques known to those skilled in the art. The

antibodies are substantially free of many of the adverse side effects which may be associated with other anti-viral agents such as drugs.

The antibody compositions can be made even more compatible with the host system by minimizing potential 10 adverse immune system responses. This is accomplished by removing all or a portion of the Fc portion of a foreign species antibody or using an antibody of the same species as the host animal, for example, the use of antibodies from human/human hybridomas. Humanized antibodies (i.e., nonimmunogenic in a human) may be produced, for example, by 15 replacing an immunogenic portion of an antibody with a corresponding, but nonimmunogenic portion (i.e., chimeric antibodies). Such chimeric antibodies may contain the reactive or antigen binding portion of an antibody from one 20 species and the Fc portion of an antibody (nonimmunogenic) from a different species. Examples of chimeric antibodies, include but are not limited to, non-human mammal-human chimeras, rodent-human chimeras, murine-human and rat-human chimeras (Robinson et al., International Patent Application 25 184,187; Taniguchi M., European Patent Application 171,496; Morrison et al., European Patent Application 173,494; Neuberger et al., PCT Application WO 86/01533; Cabilly et al., 1987 Proc. Natl. Acad. Sci. USA 84:3439; Nishimura et al., 1987 Canc. Res. 47:999; Wood et al., 1985 Nature 30 314:446; Shaw et al., 1988 J. Natl. Cancer Inst. 80:15553, all incorporated herein by reference).

General reviews of "humanized" chimeric antibodies are provided by Morrison S., 1985 Science 229:1202 and by Oi et al., 1986 BioTechniques 4:214.

35 Suitable "humanized" antibodies can be

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alternatively produced by CDR or CEA substitution (Jones et al., 1986 Nature 321:552; Verhoeyan et al., 1988 Science 239:1534; Biedleret al. 1988 J. Immunol. 141:4053, all incorporated herein by reference).

The antibodies or antigen binding fragments may also be produced by genetic engineering. The technology for expression of both heavy and light cain genes in <u>E</u>. coli is the subject of the PCT patent applications; publication number WO 901443, WO901443, and WO 9014424 and in Huse et al., 1989 Science 246:1275-1281.

The antibodies can also be used as a means of enhancing the immune response. The antibodies can be administered in amount similar to those used for other therapeutic administrations of antibody. For example, normal immune globulin is administered at 0.02-0.1 ml/lb body weight during the early incubation period of other viral diseases such as rabies, measles, and hepatitis B to interfere with viral entry into cells. Thus, antibodies reactive with the HCV El protein can be passively administered alone or in conjunction with another antiviral agent to a host infected with an HCV to enhance the immune response and/or the effectiveness of an antiviral drug.

Alternatively, anti-HCV E1 antibodies can be induced by administered anti-idiotype antibodies as immunogens. Conveniently, a purified anti-HCV E1 antibody preparation prepared as described above is used to induce anti-idiotype antibody in a host animal, the composition is administered to the host animal in a suitable diluent. Following administration, usually repeated administration, the host produces anti-idiotype antibody. To eliminate an immunogenic response to the Fc region, antibodies produced by the same species as the host animal can be used or the Fc region of the administered antibodies can be removed. Following induction of anti-idiotype antibody in the host animal, serum or plasma is removed to provide an antibody

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composition. The composition can be purified as described above for anti-HCV El antibodies, or by affinity chromatography using anti-HCV El antibodies bound to the affinity matrix. The anti-idiotype antibodies produced are similar in conformation to the authentic HCV El protein and may be used to prepare an HCV vaccine rather than using an HCV B1 protein.

When used as a means of inducing anti-HCV virus antibodies in an animal, the manner of injecting the antibody is the same as for vaccination purposes, namely intramuscularly, intraperitoneally, subcutaneously or the like in an effective concentration in a physiologically suitable diluent with or without adjuvant. One or more booster injections may be desirable.

The HCV E1 proteins of the invention are also 15 intended for use in producing antiserum designed for preor post-exposure prophylaxis. Here an El protein, or mixture of El proteins is formulated with a suitable adjuvant and administered by injection to human volunteers, according to known methods for producing human antisera. Antibody response to the injected proteins is monitored, during a several-week period following immunization, by periodic serum sampling to detect the presence of anti-HCV El serum antibodies, using an immunoassay as described

25 The antiserum from immunized individuals may be administered as a pre-exposure prophylactic measure for individuals who are at risk of contracting infection. antiserum is also useful in treating an individual postexposure, analogous to the use of high titer antiserum against hepatitis B virus for post-exposure prophylaxis. 30

For both in vivo use of antibodies to HCV viruslike particles and proteins and anti-idiotype antibodies and diagnostic use, it may be preferable to use monoclonal antibodies. Monoclonal anti-HCV E1 protein antibodies or anti-idiotype antibodies can be produced as follows.

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spleen or lymphocytes from an immunized animal are removed and immortalized or used to prepare hybridomas by methods known to those skilled in the art. (Goding, J.W. 1983. Monoclonal Antibodies: Principles and Practice, Pladermic Press, Inc., NY, NY, pp. 56-97). To produce a human-human 5 hybridoma, a human lymphocyte donor is selected. A donor known to be infected with HCV (where infection has been shown for example by the presence of anti-virus antibodies in the blood or by virus culture) may serve as a suitable lymphocyte donor. Lymphocytes can be isolated from a 10 peripheral blood sample or spleen cells may be used if the donor is subject to splenectomy. Epstein-Barr virus (EBV) can be used to immortalize human lymphocytes or a human fusion partner can be used to produce human-human hybridomas. Primary in vitro immunization with peptides can also be used in the generation of human monoclonal 15 antibodies.

Antibodies secreted by the immortalized cells are screened to determine the clones that secrete antibodies of the desired specificity. For monoclonal anti-El antibodies, the antibodies must bind to HCV El protein. For monoclonal anti-idiotype antibodies, the antibodies must bind to anti-El protein antibodies. Cells producing antibodies of the desired specify are selected.

The present invention also relates to the use of single-stranded antisense poly- or oligonucleotides derived from nucleotide sequences substantially homologous to those shown in SEQ ID NOs:1-51 to inhibit the expression of hepatitis C E1 genes. By substantially homologous as used throughout the specification and claims to describe the nucleic acid sequences of the present invention, is meant a level of homology between the nucleic acid sequence and the SEQ ID Nos. referred to in that sentence. Preferably, the level of homology is in excess of 80%, more preferably in excess of 90%, with a preferred nucleic acid sequence being in excess of 95% homologous with the DNA sequence shown in

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the indicated SEQ ID NO. These anti-sense poly- or oligonucleotides can be either DNA or RNA. The targeted sequence is typically messenger RNA and more preferably, a single sequence required for processing or translation of the RNA. The anti-sense poly- or oligonucleotides can be conjugated to a polycation such as polylysine as disclosed in Lemaitre, M. et al. ((1989) Proc. Natl. Acad. Sci. USA 84:648-652) and this conjugate can be administrated to a mammal in an amount sufficient to hybridize to and inhibit the function of the messenger RNA.

The present invention further relates to multiple computer-generated alignments of the nucleotide and deduced amino acid sequences shown in SEQ ID NOs:1-102. Computer analysis of the nucleotide sequences shown in SEQ ID NOs:1-51 and of the deduced amino acid sequences shown in SEQ ID NOs:52-102 can be carried out using commercially available computer programs known to one skilled in the art.

In one embodiment, computer analysis of SEQ ID NOs:1-51 by the program GENALIGN (Intelligenetics, Inc. Mountainview, CA) results in distribution of the 51 sequences into twelve genotypes based upon the degree of variation of the sequences. For the purposes of the present invention, the nucleotide sequence identity of E1 cDNAs of HCV isolates of the same genotype is in the range of about 85% to about 100% whereas the identity of E1 cDNA sequences of different genotypes is in the range of about 50% to about 80%.

The grouping of SEQ ID NOs:1-51 into twelve HCV genotypes is shown below.

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٥	SEO ID NOs:	Genotypes
5	1-8 9-25 26-29 30-33 34 35-39 40 41 42-43 44	I/la II/lb III/2a IV/2b 2c V/3a 4a 4b 4c 4d 5a 6a

10 For those genotypes containing more than one E1 nucleotide sequence, computer alignment of the constituent nucleotide sequences of the genotype was conducted using GENALIGN in order to produce a consensus sequence for each These alignments and their resultant consensus 15 sequences are shown in Figures 1A-G for the seven genotypes (I/1a, II/1b, III/2a, IV/2b, V/3a, 4c and 5a) which comprise more than one nucleotide sequence. Further alignment of the consensus sequences of Figures 1A-G with SEQ ID NO:34 (genotype 2c), SEQ ID NO:40 (genotype 4a), SEQ 20 ID NO:41 (genotype 4b), SEQ ID NO:44 (genotype 4d) and SEQ ID NO:51 (genotype 6a) produces a consensus sequence for all twelve genotypes as shown in Figure 1H. The multiple alignments of nucleotide sequences shown in Figures 1A-H serve to highlight regions of homology and non-homology 25 between different sequences and hence, can be used by one skilled in the art to design oligonucleotides useful as reagents in diagnostic assays for HCV.

Examples of purified and isolated oligonucleotide sequences provided by the present invention are shown as SEQ ID NOs:109-135. The oligonucleotides shown in SEQ ID NOs:109-135 are useful as "genotype-specific" primers and probes since these oligonucleotides can hybridize specifically to the nucleotide sequence of the E1 gene of HCV isolates belonging to a single genotype. The genotype-specificity of the oligonucleotides shown in SEQ ID

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NOS:109-135 is as follows: SEQ ID NOS:109-110 are specific for genotype I/la; SEQ ID NOS:111-112 are specific for genotype II/lb; SEQ ID NOS:113-114 are specific for genotype III/2a; SEQ ID NOS:115-116 are specific for genotype IV/2b; SEQ ID NOS:117-119 are specific for genotype 2c; SEQ ID NOS:120-122 are specific for genotype V/3a; SEQ ID NOS:123-124 are specific for genotype 4a; SEQ ID NOS:125-125 are specific for genotype 4b; SEQ ID NOS:127-128 are specific for genotype 4c; SEQ ID NOS:129-130 are specific for genotype 4d; SEQ ID NOS:131-132 are

specific for genotype 5a and SEQ ID NOs:133-135 are specific for genotype 6a.

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The oligonucleotides of this invention can be synthesized using any of the known methods of oligonucleotide synthesis (e.g., the phosphodiester method of Agarwal et al. 1972, Agnew. Chem. Int. Ed. Engl. 11:451, the phosphotriester method of Hsiung et al. 1979, Nucleic Acids Res 6:1371, or the automated diethylphosphoramidite method of Baeucage et al. 1981, Tetrahedron Letters 22:1859-1862), or they can be isolated fragments of naturally occurring or cloned DNA. In addition, those skilled in the art would be aware that oligonucleotides can be synthesized by automated instruments sold by a variety of manufacturers or can be commercially custom ordered and prepared. In a preferred embodiment, SEQ ID NO:103 through SEQ ID NO:135, are synthetic oligonucleotides.

The present invention also relates to a method for detecting the presence of HCV in a mammal, said method comprising analyzing the RNA of a mammal for the presence of hepatitis C virus.

30 The RNA to be analyzed can be isolated from serum, liver, saliva, lymphocytes or other mononuclear cells as viral RNA, whole cell RNA or as poly(A) + RNA.

Whole cell RNA can be isolated by methods known to those skilled in the art. Such methods include extraction of RNA by differential precipitation (Birnbiom, H.C. (1988)

- Nucleic Acids Res., 16:1487-1497), extraction of RNA by organic solvents (Chomczynski, P. et al. (1987) Anal.

  Biochem., 162:156-159) and extraction of RNA with strong denaturants (Chirgwin, J.M. et al. (1979) Biochemistry, 18:5294-5299). Poly(A) \*\* RNA can be selected from whole cell
- RNA by affinity chromatography on oligo-d(T) columns (Aviv, H. et al. (1972) Proc. Natl. Acad. Sci., 69:1408-1412). A preferred method of isolating RNA is extraction of viral RNA by the quanidium-phenol-chloroform method of Bukh et al. (1992a).
- The methods for analyzing the RNA for the presence of HCV include Northern blotting (Alwine, J.C. et al. (1977) Proc. Natl. Acad. Sci., 74:5350-5354), dot and slot hybridization (Kafatos, F.C. et al. (1979) Nucleic Acids Res., 7:1541-1522), filter hybridization (Hollander,
- M.C. et al. (1990) Biotechniques; 9:174-179), RNase protection (Sambrook, J. et al. (1989) in "Molecular Cloning, A Laboratory Manual", Cold Spring Harbor Press, Plainview, NY) and reverse-transcription polymerase chain reaction (RT-PCR) (Watson, J.D. et al. (1992) in
- "Recombinant DNA" Second Edition, W.H. Freeman and Company, New York). A preferred method is RT-PCR. In this method, the RNA can be reverse transcribed to first strand cDNA using a primer or primers derived from the nucleotide sequences shown in SEQ ID NOs:1-51. A preferred primer for
- reverse transcription is that shown in SEQ ID NO:104. Once the cDNAs are synthesized, PCR amplification is carried out using pairs of primers designed to hybridize with sequences in the HCV E1 cDNA which are an appropriate distance apart (at least about 50 nucleotides) to permit amplification of
- the cDNA and subsequent detection of the amplification product. Each primer of a pair is a single-stranded oligonucleotide of about 20 to about 60 bases in length where one primer (the "upstream" primer) is complementary to the original RNA and the second primer (the "downstream"
- 35 primer) is complementary to the first strand of cDNA

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generated by reverse transcriptions of the RNA. The target sequence is generally about 100 to about 300 base pairs long but can be as large as 500-1500 base pairs. Optimization of the amplification reaction to obtain sufficiently specific hybridization to the E1 nucleotide sequence is well within the skill in the art and is preferably achieved by adjusting the annealing temperature.

In one embodiment, the primer pairs selected to amplify E1 cDNAs are universal primers. By "universal", as used to describe primers throughout the claims and specification, is meant those primer pairs which can amplify E1 gene fragments derived from an HCV isolate belonging to any one of the twelve genotypes of HCV described herein. Purified and isolated universal primers are used in Example 1 of the present invention and are shown as SEQ ID NOs:103-108 where SEQ ID NOs:103 and 104 represent one pair of primers, SEQ ID NOs:105 and 106 represent a second pair of primers and SEQ ID NOs:107-108 represent a third pair of primers.

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In an alternative embodiment, primer pairs 20 selected to amplify E1 cDNAs are genotype-specific primers. In the present invention, genotype-specific primer pairs can readily be derived from the following genotype-specific nucleotide domains: nucleotides 197-238 and 450-480 of the consensus sequence of genotype I/la shown in Figure 1A; 25 nucleotides 197-238 and 450-480 of the consensus sequence of genotype II/1b shown in Figure 1B; nucleotides 199-238 and 438-480 of the consensus sequence of genotype III/2a shown in Figure C; nucleotides 124-177 and 450-480 of the consensus sequence of genotype TV/2b shown in Figure 1D; nucleotides 124-177, 193-238 and 436-480 of SEQ ID NO:34 30 (genotype 2C); nucleotides 168-207, 294-339 and 406-480 of the consensus sequence of genotype V/3a shown in Figure 1E; nucleotides 145-183 and 439-480 of SEQ ID NO:40 (genotype 4a); nucleotides 168-207 and 432-480 of SEQ ID NO:41 35 (genotype 4b); nucleotides 130-183 and 450-480 of the

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consensus sequence of genotype 4c shown in Figure 1F; nucleotides 130-183 and 450-480 of SEQ ID NO:44 (genotype 4d); nucleotides 166-208 and 437-480 of the consensus sequence of genotype 5a shown in Figure 1b and nucleotides 168-207, 216-252 and 429-480 of SEQ ID NO:51 (genotype 6a). 5 One skilled in the art would readily appreciate that in a pair of genotype-specific primers, each primer is derived from different genotype-specific nucleotide domains indicated above for a given genotype. Also, as described earlier, it is understood by one skilled in the art that 10 each pair of primers comprises one primer which is complementary to the original viral RNA and the other which is complementary to the first strand of cDNA generated by reverse transcription of the viral RNA. For example, in a pair of genotype-specific primers for genotype 4b, one primer would have a nucleotide sequence derived from region 15 168-207 of SEQ ID NO:40 and the other primer would have a nucleotide sequence which is the complement of region 432-480 of SEQ ID NO:40. One skilled in the art would readily recognize that such genotype specific domains would also be 20 useful in designing oligonucleotides for use as genotypespecific hybridization probes. Indeed, the sequences of such genotype-specific hybridization probes are disclosed later in the specification.

The amplification products of PCR can be detected either directly or indirectly. In one embodiment, direct detection of the amplification products is carried out via labelling of primer pairs. Labels suitable for labelling the primers of the present invention are known to one skilled in the art and include radioactive labels, biotin, avidin, enzymes and fluorescent molecules. The derived labels can be incorporated into the primers prior to performing the amplification reaction. A preferred labelling procedure utilizes radiolabeled ATP and T4 polynucleotide kinase (Sambrook, J. et al. (1989) in "Molecular Cloning, A Laboratory Manual", Cold Spring

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Harbor Press, Plainview, NY). Alternatively, the desired label can be incorporated into the primer extension products during the amplification reaction in the form of one or more labelled dNTPs. In the present invention, the labelled amplified PCR products can be detected by agarose gel electrophoresis followed by ethidum bromide staining and visualization under ultraviolet light or via direct sequencing of the PCR-products.

In yet another embodiment, unlabelled amplification products can be detected via hybridization with labelled nucleic acid probes radioactively labelled or, labelled with biotin, in methods known to one skilled in the art such as dot and slot blot hybridization (Kafatos, F.C. et al. (1979) or filter hybridization (Hollander, M.C. et al. (1990)).

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In one embodiment, the nucleic acid sequences used as probes are selected from, and substantially homologous to, SEQ ID NOs:1-51. Such probes are useful as universal probes in that they can detect in PCR-amplification products of E1 cDNAs of an HCV isolate belonging to any of the twelve HCV genotypes disclosed herein. The size of these probes can range from about 200 to about 500 nucleotides.

In an alternative embodiment, the present invention relates to a method for determining the genotype of a hepatitis C virus present in a mammal where said method comprises:

- (a) amplifying RNA of a mammal via RT-PCR to produce amplification products;
- (b) contacting said products with at least one genotype-specific oligonucleotide; and
- (c) detecting complexes of said products which bind to said oligonucleotide(s).

In this method, one embodiment of said amplification step is carried out using the universal primers (SEQ ID NO:103 through SEQ ID NO:108) as disclosed

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above. In step (b) of this method, the nucleic acid sequences used as probes are substantially homologous to the sequences shown in SEQ ID NOs:109-135. The probes disclosed in SEQ ID NOs:109-135 are useful in specifically detecting PCR-amplification products of E1 cDNAs of HCV isolates belonging to one of the twelve HCV genotypes disclosed herein. In a preferred embodiment, probes having

sequences substantially homologous to the sequences shown in SEQ ID NOs:109-135 are used alone or in combination with other probes specific to the same genotype.

For example, a probe having a sequence according to SEQ ID NO:109 can be used alone or in combination with a probe having a sequence according to SEQ ID NO:110. The probes derived from SEQ ID NOs:109-135 can range in size from about 30 to about 70 nucleotides and can be synthesized as described earlier.

The nucleic acid sequence used as a probe to detect PCR amplification products of the present invention can be labeled in single-stranded or double-stranded form. Labelling of the nucleic acid sequence can be carried out 20 by techniques known to one skilled in the art. labelling techniques can include radiolabels and enzymes (Sambrook, J. et al. (1989) in "Molecular Cloning, A Laboratory Manual", Cold Spring Harbor Press, Plainview, New York). In addition, there are known non-radioactive 25 techniques for signal amplification including methods for attaching chemical moieties to pyrimidine and purine rings (Dale, R.N.K. et al. (1973) Proc. Natl. Acad. Sci., 70:2238-2242; Heck, R.F. (1968) S. Am. Chem. Soc., 90:5518-5523), methods which allow detection by chemiluminescence (Barton, S.K. et al. (1992) J. Am. Chem. Soc., 114:8736-30 8740) and methods utilizing biotinylated nucleic acid probes (Johnson, T.K. et al. (1983) Anal. Biochem., 133:126-131; Erickson, P.F. et al. (1982) <u>J. of Immunology</u> Methods, 51:241-249; Matthaei, F.S. et al. (1986) Anal. Biochem., 157:123-128) and methods which allow detection by 35

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fluorescence using commercially available products.

The present invention also relates to computer analysis of the amino acid sequences shown in SEQ ID NOs:52-102 by the program GENALIGN. This analysis groups the 51 amino acid sequences shown in SEQ ID NOs:52-102 into the twelve genotypes disclosed earlier in this application based upon the degree of variation of the amino acid sequences. For the purposes of the present invention, the amino acid sequence identity of E1 amino acid sequences of the same genotype ranges from about 85% to about 100% whereas the identity of E1 sequences of different genotypes ranges from about 45% to about 80%.

The grouping of SEQ ID NOs:52-102 into the twelve HCV genotypes is shown below:

15	SEO ID NOs:	<u>Genotypes</u>
20	52-59 60-76 77-80 81-84 85 86-90 91 92 93-94 95 96-101	I/1a II/1b III/2a IV/2b 2c V/3a 4a 4b 4c 4d 5a
	102	6a

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25 For those genotypes containing more than one E1 amino acid sequence, computer alignment of the constituent sequences of each genotype was conducted using the computer program GENALIGN in order to produce a consensus sequence for each genotype. These alignments and their resultant consensus sequences are shown in Figures 2A-G for the seven genotypes (I/la, II/lb, III/2a, IV/2b, V/3a, 4c and 5a) which comprise more than one sequence. Further alignment of the consensus sequences shown in Figures 2A-G with the amino acid sequences of SEQ ID NO:85 (genotype 2c); SEQ ID NO:91 (genotype 4a); SEQ ID NO:92 (genotype 4b); SEQ ID

NO:95 (genotype 4d) and SEQ ID NO:102 (genotype 6a) to produce a consensus amino acid sequence for all twelve genotypes is shown in Figure 2H. The multiple alignment of E1 amino acid sequences shown in Figures 2A-H serves to highlight regions of homology and non-homology between 5 amino acid sequences and hence, these alignments can readily be used by one skilled in the art to derive peptides useful in assays and vaccines for the diagnosis and prevention of HCV infection. Examples of purified and isolated peptides are provided by the present invention are 10 shown as SEQ ID NOs:136-159. These peptides are derived from two regions of the amino acid sequences shown in Figures 2A-H, amino acids 48-80 and amino acids 138-160. The peptides shown in SEQ ID NOs:136-159 are useful as genotype-specific diagnostic reagents since they are capable of detecting an immune response specific to HCV 15 isolates belonging to a single genotype. The genotypespecificity of the peptides shown in SEQ ID NOs:136-159 are as follows: SEQ ID NOs:136 and 148 are specific for genotype IV/2b; SEQ ID NOs:137 and 149 are specific for 20 genotype 2c; SEQ ID NOs:138 and 150 are specific for genotype III/2a; SEQ ID NOs:139 and 151 are specific for genotype V/a; SEQ ID NOs:140 and 152 are specific for genotype II/1b; SEQ ID NOs:141 and 153 are specific for genotype I/la; SEQ ID NOs:142 and 154 are specific for 25 genotype 4a; SEQ ID NOs:143 and 155 are specific for genotype 4c; SEQ ID NOs:144 and 156 are specific for genotype 4d; SEQ ID NOs:145 and 157 are specific for genotype 4b; SEQ ID NOs:146 and 158 are specific for genotype 5a and SEQ ID NOs:147 and 159 are specific for 30 genotype 6a. In SEQ ID NO:136, Xaa at position 22 is a residue of Ala or Thr, Xaa at position 24 is a residue of Val or Ile, Xaa at position 26 is a residue of Val or Met; in SEQ ID NO:138, Xaa at position 5 is a Ser or Thr residue, Xaa at position 11 is an Arg or Gln residue, Xaa 35 at position 12 is an Arg or Gln residue; in SEQ ID NO:139,

Xaa at position 3 is a Pro or Ser residue, Xaa at position 33 is a Leu or Met residue; in SEQ ID NO:140, Xaa at position 5 is a Thr or Ala residue, Xaa at position 13 is a Gly, Ala, Ser, Val or Thr residue, Xaa at position 14 is a Ser, Thr or Asn residue, Xaa at position 15 is a Val or Ile 5 residue, Xaa at position 16 is a Pro or Ser residue, Xaa at position 18 is a Thr or Lys residue, Xaa at position 19 is a Thr or Ala residue, Kaa at position 22 is an Arg or His residue, Xaa at position 32 is an Ala, Val or Thr residue; in SEQ ID NO:141, Xaa at position 3 is an Ala or Pro 10 residue, Xaa at position 4 is a Val or Met residue, Xaa at position 5 is a Thr or Ala residue, Xaa at position 17 is a Thr or Ala residue, Xaa at position 18 is a Thr or Ala residue, Xaa at position 23 is a His or Tyr residue; in SEQ ID NO:143, Xaa at position 10 is a Val or Ala residue, Xaa at position 11 is a Ser or Pro residue, Xaa at position 18 15 is an Asp or Glu residue Xaa at position 20 is a Leu or Ile residue; in SEQ ID NO:146, Xaa at position 3 is a Gln or His residue, Xaa at position 12 is an Asn, Ser or Thr residue, Xaa at position 13 is a Leu or Phe residue, Xaa at 20 position 23 is an Ala or Val residue; in SEQ ID NO:148, Xaa at position 16 is a Val or Ala residue, Xaa at position 18 is a Glu or Gln residue; in SEQ ID NO:150, Xaa at position 2 is an Ala or Thr residue, Xaa at position 4 is a Met or Leu residue, Xaa at position 9 is an Ala or Val residue, 25 Xaa at position 17 is an Ile or Leu residue, Xaa at position 20 is an Ile or Val residue, Xaa at position 21 is a Ser or Gly residue; in SEQ ID NO:151, Xaa at position 9 is a Val or Ile residue, Xaa at position 16 is a Leu or Val residue, Xaa at position 20 is an Ile or Leu residue; in SEQ ID NO:152, Kaa at position 2 is an Ala or Thr residue, 30 Xaa at position 6 is a Val or Leu residue, Xaa at position 12 is an Ile or Leu residue, Kaa at position 16 is a Val or Ile residue, Xaa at position 17 is a Val, Leu or Met residue, Xaa at position 19 is a Met or Val residue, Xaa at position 21 is an Ala or Thr residue; in SEQ ID NO:153, Xaa 35

residue.

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at position 2 is a Thr or Ala residue, Xaa at position 6 is a Val, Ile or Met residue, Xaa at position 12 is an Ile or Val residue, Xaa at position 16 is a Ile or Val residue; in SEQ ID NO:155, Xaa at position 5 is a Leu or Val residue, Xaa at position 21 is a Thr or Ala residue; in SEQ ID NO:158, Xaa at position 1 is a Thr or Ala residue, Xaa at position 5 is a Val or Leu residue, Xaa at position 9 is a

Those skilled in the art would be aware that the peptides of the present invention or analogs thereof can be synthesized by automated instruments sold by a variety of manufacturers or can be commercially custom-ordered and prepared. The term analog has been described earlier in the specification and for purposes of describing the peptides of the present invention, analogs can further include branched or non-linear arrangements of the peptide sequences shown in SEQ ID NOs:136-159.

Leu, Met or Val residue, Xaa at position 23 is a Gly or Ala

Alternatively, peptides can be expressed from nucleic acid sequences where such sequences can be DNA, cDNA, RNA or any variant thereof which is capable of directing protein synthesis. In one embodiment, restriction digest fragments containing a coding sequence for a peptide can be inserted into a suitable expression vector that functions in prokaryotic or eukaryotic cells. Such restriction digest fragments may be obtained from clones isolated from prokaryotic or eukaryotic sources which encode the peptide sequence.

Suitable expression vectors and methods of isolating clones encoding the peptide sequences of the present invention have previously been described.

The preferred size of the peptides of the present invention is from about 8 to about 100 amino acids in length.

The present invention further relates to the use of the peptides shown in SEQ ID NOs:136-159 in methods of

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detecting antibodies specific for HCV in biological samples. In one embodiment, at least one peptide specific for a single genotype to be used in previously described immunoassays to detect antibodies specific for a single genotype of HCV. A preferred immunoassay is ELISA.

It is understood by one skilled in the art that the diagnostic assays described herein using genotype-specific oligonucleotides or genotype-specific peptides cabe useful in assisting one skilled in the art to choose a course of therapy for the HCV-infected individual.

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In an alternative embodiment, a mixture of peptides can be used in an immunoassay to detect antibodies to any of the twelve genotypes of HCV. The mixture of peptides as disclosed herein, comprises at least one peptide selected from SEQ ID NOs:140-141 and 152-153; one peptide selected from SEQ ID NOs:136, 138, 148 and 150; one peptide selected from SEQ ID NOs:142-145 and 154-157; one peptide selected from SEQ ID NOs:146 and 158; one peptide selected from SEQ ID NOs:139 and 151; one peptide selected from SEQ ID NOs:138 and 150 and one peptide selected from SEQ ID NOs:140 and 159. In a preferred embodiment, the peptides of the present invention can be used in an ELISA assay as described previously for E1 proteins.

The peptides or analogs thereof may be prepared in the form of a kit, alone or in combinations with other reagents such as secondary antibodies, for use in immunoassay. In addition, since genotype-specific peptides shown in SEQ ID NOs:136-159 are derived from two variable regions in the E1 protein, amino acids 48-80 (SEQ ID NOs:136-147) and amino acids 138-160 (SEQ ID NOs:148-159), one skilled in the art would recognize that these peptides would be useful as vaccines against hepatitis C. In the present invention, a peptide from SEQ ID NOs:136-159 can be used alone or in combination with other peptides shown therein as immunogens in the vaccine. Formulations suitable for administering the peptide(s) of the present

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invention, routes of administration, pharmaceutical compositions comprising the peptid s and so forth are the same as those previously described for recombinant E1 proteins. In addition, as described for E1 proteins, the peptide(s) can also be used to prepare antibodies to HCV-E1 protein.

The peptides of the present invention may also be supplied in the form of a kit, alone, or in the form of a pharmaceutical composition as described above for E1 proteins recombinant.

Any articles or patents referenced herein are incorporated by reference. The following examples illustrate various aspects of the invention but are in no way intended to limit the scope thereof.

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#### MATERIALS

Serum used in these examples was obtained from 84 anti-HCV positive individuals that were previously found to be positive for HCV RNA in a cDNA PCR assay with primer set a from the 5' NC region of the HCV genome (Bukh, J. et al. (1992 (b)) Natl. Acad. Sci. USA 89:4942-4946). samples were from 12 countries: Denmark (DK); Dominican Republic (DR); Germany (D); Hong Kong (HK); India (IND); Sardinia, Italy (S); Peru (P); South Africa (SA); Sweden (SW); Taiwan (T); United States (US); and Zaire (Z).

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### Example 1

Identification of the DNA Sequence of the El Gene of 51 Isolates of HCV via RT-PCR Analysis of Viral RNA Using Universal Primers

15 Viral RNA was extracted from 100  $\mu$ l of serum by the guanidinium-phenol-chloroform method and the final RNA solution was divided into 10 equal aliquots and stored at -80°C as described (Bukh, et al. (1992 (a)). The sequences of the synthetic oligonucleotides used in the RT-PCR assay, 20 deduced from the sequence of HCV strain H-77 (Ogata, N. et al. (1991) Proc. Natl. Acad. Sci. USA 88:3392-3396), are shown as SEQ ID NOs:103-108. One aliquot of the final RNA solution, equivalent to 10  $\mu l$  of serum, was used for cDNA synthesis that was performed in a 20  $\mu$ l reaction mixture using avian myeloblastosis virus reverse transcriptase (Promega, Madison, WI) and SEQ ID NO:104 as a primer. resulting cDNA was amplified in a "nested" PCR assay by Tag DNA polymerase (Amplitaq, Perkin-Elmer/Cetus) as described previously (Bukh et al. (1992a)) with primer set e (SEQ ID NOs:103-106). Precautions were taken to avoid contamination with exogenous HCV nucleic acid (Bukh et al. 1992a)), and negative controls (normal, uninfected serum) were interspersed between every test sample in both the RNA extraction and cDNA PCR procedures. No false positive results were observed in the analysis. In most instances,

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amplified DNA (first or second PCR products) was reamplified with primers SEQ ID NO:107 and SEQ ID NO:108 prior to sequencing since these two primers contained EcoR1 sites which would facilitate future cloning of the E1 gene. Amplified DNA was purified by gel electrophoresis followed 5 by glass-milk extraction (Geneclean, BIO 101, LaJolla, CA) and both strands were sequenced directly by the dideoxynucleotide chain termination method (Bachman, B. et al. (1990) Nucl. Acids Res. 18:1309)) with phage T7 DNA polymerase (Sequenase, United States Biochemicals, 10 Cleveland, OH), [alpha 35S]dATP (Amersham, Arlington Heights, IL) or [alpha 33P] dATP (Amersham or DuPont, Wilmington, DE) and sequencing primers. RNA extracted from serum containing HCV strain H-77, previously sequenced by Ogata, N. et al. (1991), was amplified with primer set e 15 (SEQ ID NOs:103-106) and sequenced in parallel as a The nucleotide sequences of the envelope 1 (E1) gene of all 51 HCV isolates are shown as SEQ ID NOs:1 - 51. In all 51 HCV isolates, the E1 gene was exactly 576 nucleotides in length and did not have any in-frame stop 20 codons.

#### Example 2

Computer Analysis of the Nucleotide and Deduced Amino Acid Sequences of the E1 Gene of the 51 HCV Isolates

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Multiple computer-generated alignments of the nucleotide (SEQ ID NOs:1-51, Figures 1A-H) and deduced amino acid sequences (SEQ ID NOs:52-102, Figures 2A-H) of the cDNAs of the 51 HCV isolates constructed using the computer program GENALIGN (Miller, R.H. et al. (1990) Proc. Natl. Acad. Sci. USA 87:2057-2061) resulted in the 51 HCV isolates being divided into twelve genotypes based upon the degree of variation of the E1 gene sequence as shown in table 1.

Biochemistry: Bukh et al.

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Table 1. Percent nucleotide (nt) and amino acid (aa) sequence identify of the E1 gene among the 12 HCV genotypes.

_		_					_		_					_
ij	1/18	IJ1b	Ш/2а	IV/2b	22	(V)/3a	48	4	5	4d	Sa	ба		小 一
68	62.2-63.9	61.6-63.0	55.0-56.8	53.6-55.2	57.6	58.0-58.9	62.0	62.7	63.0-64.4	64.1	60.6-63.2			
Sa	67.7-69.4 62.3-67.2	63.0-65.5 62.2-66.5	58.7-61.3 56.6-60.8	53.5-56.6	56.9-57.1	61.8-64.4	62.8-64.6	63.9-64.6	62.7-64.8 63.0-64.4	64.4-66.1	90.1-95.7		92.7-97.4	62.0-63.5
4 64	67.7-69.4	63.0-65.5	58.7-61.3	57.5-59.0	58.9	62.3-63.9	74.8	72.0	77.6-78.6	:		:	69.3-71.4	66.7
4c	62.7-64.4	61.6-65.1	59.7-63.4	57.1-59.9	58.0-58.3	60.9-62.5	75.5-78.0	74.0-74.8	90.1		9.68	82.8	67.7-71.4	66.1-67.2
4p	64.9-66.8	63.4-65.8	58.9-60.4	56.4-57.6	58.5	62.7-64.1	74.8	1		:	79.2-80.2	77.6	65.1-67.2	62.5
4a	63.9-67.2	60.9-63.7	61.5-62.7	58.9-60.8	59.2	64.4-65.3			1	76.0	77.1-81.3	78.1	67.2-68.2	66.1
(V)/3a	63.0-66.3	63.9-67.2	58.09-0.85	56.3-58.3	57.5-58.2	93.8-99.1		94.3-98.4	66.1-68.8	62.0-64.6	63.0-65.6	63.5-64.6	60.4-64.1	57.8-58.9
20	60.8-62.8	60.1-61.5	72.7-73.6	67.5-68.9	•	Skutani (1922)	-	52.1-53.6	58.3	53.6	54.7-58.3	54.2	54.2-56.3	50.5
IV/2b	56.1-58.3	53.8-57.5	69.1-71.0	92.7-95.0		93.8-96.4	67.7-69.8	54.2-56.8	58.9-60.4	52.1-53.1	54.2-58.3	55.2-55.7	50.5-53.1	49.0-50.5
Ш/2а	59.2-63.7	58.3-62.2	88.0-91.3		89.1-92.7	69.3-72.9	74.5-77.1	54.7-58.9	62.0-63.0	53.6-56.3	55.2-61.5	56.3-58.9	52.6-57.3	49.0-51.0
II/1b	72.0-76.2	6.76-6.88		90.1-97.9	52.6-56.8	51.0-54.2	52.6-55.7	8.07-7.99	64.6-67.2	66.1-70.3	64.6-69.3	66.7-70.3	64.1-70.3	62.5-65.6
I/1a	89.9-97.6		91.1-98.4	75.5-80.7	58.3-64.6	54.2-56.8	56.3-60.4	64.1-68.8	69.3-73.4	66.7-69.3	66.1-72.9	73.4-75.5	66.1-73.4	64.6-65.6
	201913	88:	I/1a	П/16	Ш/2а	IV/2b	2c	(V)/3a	4a	<del>\$</del>	40	4q	Sa	6а

Nuclectide sequences analyzed in compiling the above table are shown in SEQ ID NOs:1-51 while the amino acid sequences analyzed are shown in SEQ ID NOs:52-102. The grouping of SEQ ID NOs: into genotypes is previously described in the specification.

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The nucleotide and amino acid sequence identity of HCV isolates of the same genotype was in the range of 88.0-99.1% and 89.1-98.4%, respectively, whereas that of HCV isolates of different genotypes was in the range of 53.5-78.6% and 49.0-82.8%, respectively. 5 differences are similar to those found when comparing the envelope gene sequences of the various serotypes of the related flaviviruses, as well as other RNA viruses. microheterogenicity in a sequence was observed, defined as more than one prominent nucleotide at a specific position, 10 the nucleotide that was identical to that of the HCV prototype (HCV1, Choo et al. (1989)) was reported if possible. Alternatively, the nucleotide that was identical to the most closely related isolate is shown.

Analysis of the consensus sequence of the E1 15 protein of the 51 HCV isolates from this study demonstrated that a total of 60 (30.3%) of the 192 amino acids of the E1 protein were invariant among these isolates (Fig. 3). impressive, all 8 cysteine residues as well as 6 of 8 proline residues were invariant. The most abundant amino acids (e.g. alanine, valine and leucine) showed a very low 20 degree of conservation. The consensus sequence of the E1 protein contained 5 potential N-linked glycosylation sites. Three sites at positions 209, 305 and 325 were maintained in all 51 HCV isolates. A site at position 196 was maintained in all isolates except the sole isolate of 25 genotype 2c. Also, a site at position 234 was maintained in all isolates except one isolate of genotype I/1a, all four isolates of genotype IV/2b and the sole isolate of genotype 6a. Conversely, only genotype IV/2b isolates had a potential glycosylation site at position 233. Further 30 analysis revealed a highly conserved amino acid domain (aa 302-328) in the E1 protein with 20 (74.1%) of 27 amino acids invariant among all 51 HCV isolates. It is possible that the 5' and 3' ends of this domain are conserved due to important cysteine residues and N-linked glycosylation 35

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sites. The central sequence, 5'-GHRMAWDMM-3' (aa 315-323), may be conserved due to additional functional constraints on the protein structure. Finally, although the amino acid sequence surrounding the putative E1 protein cleavage site was variable, an amino acid doublet (GV) at position 380 was invariant among all HCV isolates.

A dendrogram of the genetic relatedness of the E1 protein of selected HCV isolates representing the 12 genotypes is shown in Fig. 4. This dendrogram was constructed using the program CLUSTAL (Weiner, A.J. et al. 10 (1991) Virology 180:842-848) and had a limit of 25 sequences. The scale showing percent identity was added based upon manual calculation. From the 51 HCV isolates for which the complete sequence of the E1 gene region was obtained, 25 isolates representing the twelve genotypes were selected for analysis as follows. Among isolates with 15 genotype I/1a (SEQ ID NOs:52-59), as well as among isolates with genotype II/1b (SEQ ID NOs:60-76) the two isolates with the lowest amino acid identity within each genotype were included. Among isolates of genotype IV/2b, isolate DK8 (SEQ ID NO:81) that has an amino acid identity of 96.4% 20 to isolate T8 (SEQ ID NO:84) was excluded. Among isolates of genotype V/3a, isolates S2 (SEQ ID NO:88) and S54 (SEQ ID NO:90) that both shared 97.9 % of the amino acids of isolates HK10 (SEQ ID NO:87) and S52 (SEO ID NO:89) were excluded. Finally, among isolates of genotype VI, isolates 25 SA4 (SEQ ID NO:97) and SA5 (SEQ ID NO:98) with an amino acid identity to isolate SA7 (SEQ ID NO:100) of 96.4% and 95.8%, respectively were excluded. This dendrogram in combination with the analysis of the E1 gene sequence of 51 30 HCV isolates in Table 1 demonstrates extensive heterogeneity of this important gene.

The worldwide distribution of the 12 genotypes among 74 HCV isolates is depicted in Fig. 5. The complete E1 gene sequence was determined in 51 of these HCV isolates (SEQ ID NOs:1-51), including 8 isolates of genotype I/1a,

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17 isolates of genotype II/1b and 26 isolates comprising genotypes III/2a, IV/2b, 2c, 3a, 4a-4d, 5a and 6a. remaining 23 isolates, all of genotypes I/1a and II/1b, the genotype assignment was based on a partial E1 gene sequence since they did not represent additional genotypes in any of 5 the 12 countries. The number of isolates of a particular genotype is given in each of the 12 countries studied. Of the twelve genotypes, genotypes I/la and II/lb were the most common accounting for 48 (65%) of the 74 isolates. Analysis of the E1 gene sequences available in the GenBank 10 data base at the time of this study revealed that all 44 such sequences were of genotypes I/la, II/lb, III/2a and Thus, based upon El gene analysis, 8 new genotypes of HCV have been identified.

Also of interest, different HCV genotypes were frequently found in the same country, with the highest number of genotypes (five) being detected in Denmark. Of the twelve genotypes, genotypes I/la, II/lb, III/2a, IV/2b and V/3a were widely distributed with genotype II/lb being identified in 11 of 12 countries studied (Zaire was the only exception). In addition, while genotypes I/la and II/lb were predominant in the Americas, Europe and Asia, several new genotypes were predominant in Africa.

It was also found that genotypes I/la, II/lb, III/2a, IV/2b and V/3a of HCV were widely distributed around the world, whereas genotypes 2c, 4a, 4b, 4d, 5a and 6a were identified only in discreet geographical regions. For example, the majority of isolates in South Africa comprised a new genotype (5a) and all isolates in Zaire comprised 3 new closely related genotypes (4a, 4b, 4c). These genotypes were not identified outside Africa.

#### Example 3

Detection by ELISA Based on Antigen from Insect Cells Expressing Complete E1 Protein

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(SEQ ID NO:1) encoding the complete E1 protein of SEQ ID NO:52 is subcloned into pBlueBac - Transfer vector (Invitrogen) using standard subcloning procedures. The resultant recombinant expression vector is cotransfected into SF9 insect cells (Invitrogen) by the Ca precipitation method according to the Invitrogen protocol.

ELISA Based on Infected SF9 cells.  $5 \times 10^6$  SF9 cells infected with the above-described recombinant expression vector are resuspended in 1 ml of 10 mM Tris-HCl, pH 7.5, 0.15M NaCl and are then frozen and thawed 3 times. 10 ul of this suspension is dissolved in 10 ml of carbonate buffer (pH 9.6) and used to cover one flexible microtiter assay plate (Falcon). Serum samples are diluted 1:20, 1:400 and 1:8000, or 1:100, 1:1000 and 1:10000. Blocking and washing solutions for use in the ELISA assay are PBS containing 10% fetal calf serum and 0.5% gelatin (blocking solution) and PBS with 0.05% Tween -20 (Sigma, St.Louis, MO) (washing solution). As a secondary antibody, peroxidase-conjugated goat IgG fraction to human IgG or horse radish peroxidase-labelled goat anti-Old or anti-New World monkey immunoglobulin is used. The results are determined by measuring the optical density (O.D.) at 405 nm.

To determine if insect cells-derived E1 protein representing genotype I/a of HCV could detect anti-HCV antibody in chimpanzees infected with genotype I/la of HCV, three infected chimpanzees are examined. The serum of all 3 chimpanzees are found to seroconvert to anti-HCV.

# Example 4

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# Use of the Complete E1 Protein as a Vaccine

Mammals are immunized with purified or partially purified El protein in an amount sufficient to stimulate the production of protective antibodies. The immunized mammals challenged with various genotypes of HCV are

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° protected.

It is understood by one skilled in the art that the recombinant El protein used in the above vaccine can also be used in combination with other recombinant El proteins having an amino acid sequence shown in SEQ ID NOs:52-102.

#### Example 5

Determination of the Genotype of an HCV Isolate Via Hybridization of Genotype-Specific Oligonucleotides to RT-PCR Amplification Products.

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Viral RNA is isolated from serum obtained from a mammal and is subjected to RT-PCR as in Example 1. Following amplification, the amplified DNA is purified as described in Example 1 and aliquots of 100 mg of amplification product are applied to twelve dots on a nitrocellulose filter set in a dot blot apparatus. The twelve dots are then cut into separate dots and each dot is hybridized to a <sup>32</sup>p-labelled oligonucleotide specific for a single genotype of HCV. The oligonucleotides to be used as hybridization probes are selected from SEQ ID NOS:109-135.

#### Example 6

# ELISA Based on Synthetic Peptides Derived From El cDNA Sequences

Synthetic peptides specific for genotype I/la and having amino acid sequences according to SEQ ID NOs:136-148 are placed in 0.1% PBS buffer and 50ul of lmg/ml of peptide is used to cover each well of the microtiter assay plate. Serum samples from two mammals infected with genotype I/la HCV and from one mammal infected with genotype 5a HCV are diluted as in Example 3 and the ELISA is carried out as in Example 3. Both mammals infected with genotype I HCV react positively with peptides while the mammal infected with genotype 5a HCV exhibit no reactivity.

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## Example 7

# Use of the El Peptides as a Vaccine

Since the E1 genotype-specific peptides of the present invention are derived from two variable regions in the complete E1 protein, there exists support for the use of these peptides as a vaccine to protect against a variety of HCV genotypes. Mammals are immunized with peptide(s) selected from SEQ ID NOs: 136-159 in an amount sufficient to stimulate production of protective antibodies. The immunized mammals challenged with various genotypes of HCV are protected.

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0	(1)	GENERAL	INFORMATION:
		(i)	APPLICANTS: BUKH, J., MILLER, R.H. AND PURCELL, R.H.
5	·	(ii)	TITLE OF INVENTION: NUCLEOTIDE AND DEDUCED AMINO ACID SEQUENCES OF THE ENVELOPE 1 GENE OF 51 ISOLATES OF HEPATITIS C AND THE USE OF REAGENTS DERIVED FROM THESE SEQUENCES IN DIAGNOSTIC METHODS AND VACCINES
		(iii)	NUMBER OF SEQUENCES: 159
10		(iv)	CORRESPONDENCE ADDRESS: (A) ADDRESSEE: MORGAN & FINNEGAN (B) STREET: 345 PARK AVENUE (C) CITY: NEW YORK (D) STATE: NEW YORK (E) COUNTRY: USA (F) ZIP: 10154
15		(V)	COMPUTER READABLE FORM:  (A) MEDIUM TYPE: FLOPPY DISK  (B) COMPUTER: IBM PC COMPATIBLE  (C) OPERATING SYSTEM: PC-DOS/MS-DOS  (D) SOFTWARE: WORDPERFECT 5.1
20		(vi)	CURRENT APPLICATION DATA:  (A) APPLICATION NUMBER: PCT/US94/  (B) FILING DATE: 28-JUN-1994  (C) CLASSIFICATION:
		(vii)	PRIOR APPLICATION DATA: (A) APPLICATION NUMBER: 08/086,428 (B) FILING DATE: 29-JUN-1993
25		(viii)	ATTORNEY/AGENT INFORMATION: (A) NAME: RICHARD W. BORK (B) REGISTRATION NUMBER: 36,459 (C) REFERENCE/DOCKET NUMBER: 2026-4070
30		(ix)	TELECOMMUNICATION INFORMATION: (A) TELEPHONE: (212) 758-4800 (B) TELEFAX: (212) 751-6849 (C) TELEX: 421792
JU	(2)	INFORMAT	ION FOR SEQ ID NO:1:
35		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear

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ORIGINAL SOURCE:
           (vi)
                      (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE: DK7
           (xi)
                     SEQUENCE DESCRIPTION: SEO ID NO:1:
     TAC CAA GTG CGC AAC TCC ACG GGG CTT TAC CAT GTC ACC
     AAT GAT TGC CCT AAC TCG AGT ATC GTG TAC GAG GCG GCC
                                                                 78
 5
     GAT GCC ATC CTG CAC ACT CCG GGG TGT GTC CCT TGC GTT
                                                                 117
      CGC GAG GGT AAC GTC TCG AGG TGT TGG GTG GCG ATG ACC
                                                                 156
      CCC ACG GTG GCC ACC AGG GAT GGC AAA CTC CCC ACA GCG
                                                                 195
     CAG CTT CGA CGT CAC ATC GAT CTG CTC GTC GGG AGT GCC
                                                                 234
     ACC CTC TGT TCG GCC CTC TAC GTG GGG GAC CTG TGC GGG
                                                                273
     TCT GTC TTT CTT GTC GGT CAA CTG TTT ACC TTC TCT CCC
                                                                312
     AGG CGC CAC TGG ACG ACG CAA GGC TGC AAT TGT TCT ATC
                                                                351
10
     TAT CCT GGC CAT ATA ACG GGT CAC CGC ATG GCG TGG GAT
                                                                390
     ATG ATG AAC TGG TCC CCT ACC ACG GCG TTG GTA GTA
                                                               429
     GCT CAG CTG CTC CGG ATC CCG CAA GCC ATC TTG GAC ATG
                                                               468
     ATC GCT GGT GCT CAC TGG GGA GTC CTG GCG GGC ATA GCG
                                                               507
     TAT TTT TCC ATG GTG GGG AAC TGG GCG AAG GTC CTG GTA
                                                               546
     GTG CTG CTA TTT GCC GGC GTC GAC GCG
                                                                576
15
      (2)
           INFORMATION FOR SEO ID NO:2:
                     SEQUENCE CHARACTERISTICS:
           (i)
                          LENGTH: 576 base pairs
                     (A)
                          TYPE: nucleic acid
                     (B)
                          STRANDEDNESS: single
                     (C)
                          TOPOLOGY: linear
                     (D)
20
                     ORIGINAL SOURCE:
           (vi)
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE: DK9
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:2:
     TAC CAA GTA CGC AAC TCC TCG GGC CTC TAC CAT GTC ACC
                                                                 39
25
     AAT GAT TGC CCT AAC TCG AGT ATT GTG TAC GAG GCG GCC GAT GCC ATC CTG CAT TCT CCA GGG TGT GTC CCT TGC GTT
                                                                 78
                                                              117
     CGC GAG GGT AAC GCC TCG AAA TGT TGG GTG GCG GTG GCC
                                                                156
     CCC ACG GTG GCC ACC AGG GAC GGC AAG CTC CCC GCA ACG
                                                                195
     CAG CTT CGA CGT CAC ATC GAT CTG CTT GTC GGG AGC GCC
                                                                234
     ACC CTC TGC TCG GCC CTC TAT GTG GGG GAC TTG TGC GGG
                                                                273
     TCT GTC TTC CTT GTC GGC CAA CTG TTC ACC TTC TCC CCC
                                                                312
     AGA CGC CAC TGG ACA ACG CAA GAC TGC AAC TGT TCT ATC
30
                                                                351
     TAC CCC GGC CAT ATT ACG GGT CAT CGC ATG GCG TGG GAT
                                                                390
     ATG ATG ATG AAC TGG TCC CCT ACA GCA GCG CTG GTA ATG
                                                                429
     GCG CAG CTG CTC AGG ATC CCG CAG GCC ATC TTG GAC ATG
                                                                468
     ATC GCT GGT GCC CAC TGG GGA GTC CTA GCG GGC ATA GCG
                                                                507
     TAT TTC TCC ATG GTG GGG AAC TGG GCG AAG GTC GTG GTG
                                                                546
     GTA CTG TTG CTG TTT ACC GGC GTC GAT GCG
                                                                576
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35

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(2)
           INFORMATION FOR SEO ID NO:3:
                      SEQUENCE CHARACTERISTICS:
           (i)
                           LENGTH: 576 base pairs
                      (A)
                      (B)
                           TYPE: nucleic acid
                      (C)
                           STRANDEDNESS: single
                      (D)
                           TOPOLOGY: linear
 5
           (vi)
                      ORIGINAL SOURCE:
                           ORGANISM: homosapiens
                      (A)
                      (C)
                           INDIVIDUAL ISOLATE: DR1
           (xi)
                     SEQUENCE DESCRIPTION: SEO ID NO:3:
      CAC CAA GTG CGC AAC TCT ACA GGG CTT TAC CAT GTC ACC
                                                                  39
      AAT GAT TGC CCT AAT TCG AGT ATT GTG TAC GAG GCG GCC
10
                                                                  78
      GAT GCC ATC CTG CAC GCG CCG GGG TGT GTC CCT TGC GTT
                                                                  117
      CGC GAG GGT AAC GCC TCG AGG TGT TGG GTG GCG GTG ACC
                                                                 156
      CCC ACG GTG GCC ACC AGG GAC GGC AAA CTC CCC ACA ACG
                                                                 195
      CAG CTT CGA CGT CAC ATC GAC CTG CTT GTC GGG AGC GCC
                                                                 234
     ACC CTC TGC TCG GCC CTC TAC GTG GGG GAC CTG TGC GGG
TCT GTC TTC CTT GTC GGT CAA CTG TTC ACC TTT TCT CCC
                                                                 273
                                                                 312
     AGG CGC CAC TGG ACA ACG CAA GAC TGC AAT TGT TCT ATC
                                                                 351
15
      TAT CCC GGC CAT ATA ACG GGA CAC CGT ATG GCA TGG GAT
                                                                 390
     ATG ATG AAC TGG TCC CCT ACG ACA GCG CTG GTA ATG
                                                                429
     GCT CAG CTG CTC CGG ATC CCA CAA GCC ATC TTG GAC ATG
     ATC GCT GGA GCC CAC TGG GGA GTC CTA GCG GGC ATA GCG
                                                                507
                                                               546
     TAT TTC TCC ATG GTG GGG AAC TGG GCG AAG GTC GTG GTA
     GTG CTG TTG CTG TTT GCC GGC GTT GAT GCG
                                                                 576
20
           INFORMATION FOR SEO ID NO:4:
      (2)
                     SEQUENCE CHARACTERISTICS:
           (i)
                          LENGTH: 576 base pairs
                      (A)
                          TYPE: nucleic acid
                      (B)
                      (C)
                          STRANDEDNESS: single
                      (D)
                          TOPOLOGY: linear
25
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                      (C)
                          INDIVIDUAL ISOLATE: DR4
           (xi)
                     SEQUENCE DESCRIPTION: SEO ID NO:4:
     CAC CAA GTG CGC AAC TCT ACA GGG CTT TAC CAT GTC ACC
30
                                                                  39
     AAT GAT TGC CCT AAT TCG AGT ATT GTG TAC GAG GCG GCC
                                                                  78
     GAT GCC ATC CTG CAC ACG CCG GGG TGT GTC CCT TGC GTT
                                                                 117
     CGC GAG GGT AAC ACC TCG AGG TGT TGG GTG GCG GTG ACC
                                                                 156
     CCC ACG GTG GCC ACC AGG GAC GGC AAA CTC CCC ACA ACG
                                                                 195
     CAG CTC CGA CGT CAC ATC GAC CTG CTT GTC GGG AGC GCC
     ACC CTC TGC TCG GCC CTC TAC GTG GGG GAC TTG TGC GGG
     TCT GTC TTC CTT GTC GGT CAA CTG TTC ACC TTC TCT CCC
35
     AGG CAC CAC TGG ACA ACG CAA GAC TGC AAT TGT TCC ATC
```

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o	TAT CCC GGC CAT ATA ACG GGC CAC CO ATG ATG ATG AAC TGG TCC CCT ACG AC GCT CAG CTG CTC CGG ATC CCA CAA GO ATC GCT GGT GCC CAC TGG GGA GTC CT TAT TTC TCC ATG GTG GGG AAC TGG GC GTG CTG TTG CTG TTT GCC GGC GTT GA	CA GCG CTG GTA GTA 42 CC ATC TTG GAC ATG 46 TA GCG GGC ATA GCG 50 CG AAG GTC CTG GTA 54
5	(2) INFORMATION FOR SEQ ID NO:5:	
10	(B) TYPE: nucleio (C) STRANDEDNESS:	pase pairs c acid
10	(vi) ORIGINAL SOURCE: (A) ORGANISM: hom (C) INDIVIDUAL ISO	<b>-</b>
	(xi) SEQUENCE DESCRIPTION	ON: SEQ ID NO:5:
15	TAC CAA GTG CGC AAC TCC ACG GGG CT AAT GAT TGC CCT AAC TCG AGT ATT GT GAT GCT ATC CTA CAC GCT CCG GGA TC CGT GAG GGT AAC ACC TCG AGG TGT TC	TG TAC GAG ACA GCT 7: ST GTC CCT TGC GTT 11:
20	CCC ACG GTG GCC ACC AGG GAC GGC AACC CAG CTT CGA CGT TAC ATC GAT CTG CTAC CTC TGT TCG GCC CTC TAC GTG GCC CTC TGT TTT CTT GTC GGT CAG CTG TTAT CCC GGC CAT ATA ACG GGT CAT CGC ATG ATG ATG ATG AAC TGG TCC CCT ACG ACG CAG CTG CTC CGG ATC CAG CTC CTC CGG ATC CAG ACG CTC CTC CGG ATC CAA GCC CAT ATT TTC TCC ATG GTG GGA AAC TGG GCG CTC CTG GGA AAC TGG GCG CTG CTC CTG GGA AAC TGG GCG CTG CTC CTG GGA AAC TGG GCC CTG CTC CTG GGA AAC TGG GCC	AA CTC CCC GCA ACG 195 TT GTC GGG AGC GCC 234 GG GAC TTG TGC GGG 275 TT ACC TTC TCT CCC 312 GC AAT TGT TCT ATC 355 GC ATG GCA TGG GAT 396 GC GCA CTG GTA GTA 425 CC ATC TTG GAT ATG 466 TA GCG GGC ATA GCG 506 CG AAG GTC CTA GTG 546
25	GTG CTG CTA TTC GCC GGC GTT GA	AC GCG 576
23	(2) INFORMATION FOR SEQ ID NO:6:	
30	(i) SEQUENCE CHARACTERI (A) LENGTH: 576 b (B) TYPE: nucleic (C) STRANDEDNESS: (D) TOPOLOGY: lin	pase pairs cacid single
	(vi) ORIGINAL SOURCE: (A) ORGANISM: hom (C) INDIVIDUAL ISO	
	(xi) SEQUENCE DESCRIPTION	ON: SEQ ID NO:6:
35	TAC CAA GTA CGC AAC TCC ACG GGC CT	TT TAC CAT GTC ACC 39

- 54 -

5	GAT ACC ATC CTA CAC TCT C CGC GAG GGT AAC GCC TCG A CCC ACA GTT GCC ACC AGG G CAG CTT CGA CGT CAC ATC G ACC CTC TGC TCG GCC CTC T TCT GTC TTT CTT GTC AGC C AGG CGC CAC TGG ACA ACG C TAC CCC GGC CAT ATA ACG G ATG ATG ATG AAC TGG TCC C GCT CAG CTG CTC AGG GTC C ATC GCT GGT GCC CAC TGG G	GC ATT GTG TAC GAG ACG GCC         78           CG GGG TGT GTC CCT TGC GTT         117           GA TGT TGG GTG CCG GTG GCC         156           AC GGC AAA CTC CCC GCA ACG         195           AT CTG CTT GTT GGG AGC GCC         234           AT GTG GGG GAC CTG TGC GGG         273           AG CTG TTC ACT ATC TCC CCC         312           AA GAC TGC AAC TGT TCT ATC         351           GT CAC CGT ATG GCA TGG GAT         390           CT ACA ACG GCG TTG GTA ATA         429           CG CAA GCC GTC TTG GAC ATG         468           GA GTC CTA GCG GGC ATA GCG         507           AC TGG GCG AAG GTC CTG CTA         546           GC GTC GAT GCG         576
10	(2) INFORMATION FOR SEQ	ID NO:7:
15	(i) SEQUENCE C (A) LENGT (B) TYPE: (C) STRAN (D) TOPOL (vi) ORIGINAL S	HARACTERISTICS: H: 576 base pairs    nucleic acid DEDNESS: single OGY: linear
		ISM: homosapiens IDUAL ISOLATE: SW1
	(xi) SEQUENCE D	ESCRIPTION: SEQ ID NO:7:
20	AAT GAT TGC CCT AAC TCG AGGT GCC ATT CTA CAC TCT CCCGC GAG GAT GGC GCC CCG AGCC ACA GTC GCC ACT AGG GCAG CTT CGA CGT CAC ATC GCCAG CTT CGA CGT CAC ATC GCCACT AGG GCCACT CAC ATC GCACT CAC ATC ATC ATC ATC ATC ATC ATC ATC	CG GGC CTT TAC CAT GTC ACC  39 GT ATT GTG TAC GAG ACG GCC  78 CA GGG TGT GTC CCT TGC GTT  AG TGT TGG GTG GCG  AC GGC AAA CTC CCT GCA ACG  AT CTG CTT GTC GGA AGC GCC  234 AC GTG GGG GAC TTG TGC GGG  273
25	TCT GTC TTT CTC GTC AGT CAGT CAGT CAGT C	AA CTG TTC ACG TTC TCC CCC 312 AA GAC TGT AAC TGT TCT ATC 351 GT CAC CGC ATG GCA TGG GAT 390 CC ACA ACA GCG CTG GTA GTA 429 CG CAA GCC GTC TTG GAC ATG 468 GA GTC CTA GCG GGC ATA GCG 507 AC TGG GCG AAG GTC CTG ATA 546
30		5.0
•	(2) INFORMATION FOR SEQ	ID NO:8:
25	(A) LENGTI (B) TYPE:	HARACTERISTICS: H: 576 base pairs nucleic acid DEDNESS: single
35		OGY: linear

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(vi)
                     ORIGINAL SOURCE:
                          ORGANISM: homosapiens
                     (A)
                     (C)
                          INDIVIDUAL ISOLATE: US11
           (xi)
                     SEQUENCE DESCRIPTION: SEO ID NO:8:
     TAC CAA GTA CGC AAC TCC ACG GGG CTT TAC CAT GTC ACC
                                                                 39
     AAT GAT TGC CCT AAC TCG AGT ATT GTG TAC GAG GCG GCC
                                                                 78
 5
     GAT GCC ATC CTG CAC ACT CCG GGG TGT GTT CCT TGC GTT
                                                                117
     CGC GAG GGT AAC GCT TCG AGG TGT TGG GTG GCG ATG ACC
                                                                156
     CCC ACG GTG GCC ACC AGG GAC GGC AAA CTC CCC ACA ACG
                                                                195
     CAA CTT CGA CGT CAC ATC GAT CTG CTT GTC GGG AGC GCC
                                                                234
     ACC CTC TGT TCG GCC CTC TAC GTG GGG GAC CTG TGC GGG
                                                                273
     TCT GTC TTT CTT GTC GGT CAA CTG TTT ACC TTC TCT CCC
                                                               312
     AGA CGC CAC TGG ACG ACG CAG GGC TGC AAT TGT TCT ATC
                                                               351
10
     TAT CCC GGC CAT ATA ACG GGT CAC CGC ATG GCA TGG GAT
                                                               390
     ATG ATG ATG AAC TGG TCC CCT ACG GCG GCG TTG GTG GTA
                                                               429
     GCT CAG CTG CTC CGG ATC CCA CAA GCC ATC TTG GAC ATG
                                                             468
507
546
     ATC GCT GGT GCT CAC TGG GGA GTC CTA GCG GGC ATA GCG
     TAT TTC TCC ATG GTG GGG AAC TGG GCG AAG GTC CTG GTA
     GTG CTG CTA TTT GCC GGC GTC GAC GCG
                                                                576
     (2)
          INFORMATION FOR SEQ ID NO:9:
15
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH: 576 base pairs
                     (B)
                          TYPE: nucleic acid
                     (C)
                          STRANDEDNESS: single
                     (D)
                          TOPOLOGY: linear
                     ORIGINAL SOURCE:
20
          (vi)
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE: D1
           (xi)
                     SEQUENCE DESCRIPTION: SEO ID NO:9:
     TAT GAA GTG CGC AAC GTG TCC GGG GTG TAC CAT GTC ACG
                                                                39
     AAC GAC TGT TCC AAC TCG AGC ATT GTG TAT GAG ACA GCG
                                                                 78
25
     GAC ATG ATC ATG CAC ACC CCC GGG TGC GTG CCC TGC GTT
                                                                117
     CGG GAG GAC AAC TCC TCT CGC TGC TGG GTA GCG CTC ACC CCC ACG CTC GCG GCT AGG AAT GGC AAC GTC CCC ACT ACG
                                                                156
                                                                195
     GCG ATA CGA CGC CAC GTC GAT TTG CTC GTT GGG GCG GCT
                                                               234
     GCT TTC TGC TCC GCC ATG TAC GTG GGG GAT CTC TGC GGA
                                                               273
     TCT GTT TTC CTC ATC TCC CAG CTG TTC ACC CTC TCG CCT
                                                                312
     CGC CGG CAT GAG ACG GTA CAG GAG TGT AAT TGC TCA ATC
                                                               351
     TAT CCC GGC CAC GTG ACA GGT CAC CGT ATG GCT TGG GAT
                                                               390
30
     ATG ATG AAC TGG TCA CCT ACA ACA GCC TTA GTG GTA
                                                               429
     TCG CAG TTA CTC CGG ATC CCA CAA GCT GTC ATG GAC ATG
                                                               468
     GTG GCG GGC CAC TGG GGG GTC CTG GCG GGC CTC GCC
                                                               507
                                                             546
     TAC TAT TCC ATG GTG GGG AAC TGG GCT AAG GTT TTG ATT
     GTG ATG CTA CTC TTT GCT GGC GTT GAC GGC
                                                                576
```

<sup>35 (2)</sup> INFORMATION FOR SEQ ID NO:10:

PCT/US94/07320

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o	(A)	ENCE CHARACTERISTICS: LENGTH: 576 base pairs TYPE: nucleic acid STRANDEDNESS: single TOPOLOGY: linear
5	(vi) ORIG (A) (C)	
	(xi) SEQU	ENCE DESCRIPTION: SEQ ID NO:10:
10	AAT GAC TGT TCC AAC GAC ATG ATC ATG CAC CGG GAG GAC AAC TCC CCC ACG CTC GCG GCT ACA ATA CGA CGC CAC GCT TTC TGC TCC GCC TCT GTT TTC CTC GTC	GTG TCC GGG GTG TAC CAA GTC ACC  TCG AGC ATC GTG TAT GAG ACA GCG  ACC CCC GGG TGC GTG CCC TGC GTT  TCT CGC TGC TGG GTA GCG CTC ACC  AGG AAT AGC AGC GTC CCC ACT ACG  GTC GAT TTG CTC GTT GGG GCG GCT  ATG TAC GTG GGG GAT CTT TGC GGA  TCC CAG CTG TTC ACC TTC TCG CCT  39  78  78  78  78  78  78  78  78  78  7
15	TAT CCC GGC CAC GTG ATG ATG ATG AAC TGG TCG CAG TTA CTC CGG GTG GCG GGG GCC CAC TAC TAT TCC ATG GTG	GTA CAG GAA TGT AAC TGC TCA ATC  ACA GGT CAC CGC ATG GCT TGG GAT  TCG CCT ACA GCA GCC CTA GTG GTA  ATC CCA CAA GCT GTC GTG GAC ATG  TGG GGG GTC CTG GCG GGC CTC GCC  GGG AAC TGG GCT AAG GTT TTG ATT  546  GCT GGC GTC GAC GGC  576
20	(A) (B)	ENCE CHARACTERISTICS: LENGTH: 576 base pairs TYPE: nucleic acid
25	(vi) ORIG (A) (C)	STRANDEDNESS: single TOPOLOGY: linear  INAL SOURCE: ORGANISM: homosapiens INDIVIDUAL ISOLATE: DK1  ENCE DESCRIPTION: SEQ ID NO:11:
30	AAC GAC TGC TCC AAC GAC GTG ATC ATG CAT CGG GAG AAC AAC CAC CCC ACG CTC GCG GCC ACA ATA CGA CGC CAT GCT TTC TGC TCC GCT TCC GTT TTC CTC GTC	GTG TCC GGG GTG TAC CAC GTC ACA  TCA AGC ATC GTG TAT GAG GCA GTG  ACC CCA GGG TGC GTG CCC TGC GTT  TCC CGT TGC TGG GTA GCG CTC ACC  AGG AAC GCC AGC ATC CCC ACT ACG  GTC GAT TTG CTC GTT GGG GCG GCT  ATG TAC GTG GGG GAC CTC TGC GGA  TCT CAG CTG TTC ACC TTT TCA CCT  GCA CAG GAC TGC AAC TGC TCA ATC  39  78  78  78  78  78  78  78  78  78  7
35	TAT CCC GGC CAC GTT	TCA GGT CAC CGC ATG GCT TGG GAT 390 TCA CCT ACA ACA GCC CTA GTG CTA 429

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•	TCG CAG TTA CTC CGA ATC CCA CAA GCT GTC GTG GAC ATG GTG GCG GGG GCC CAC TGG GGA GTC CTG GCG GGC CTC GCC TAC TAC TCC ATG GCG GGG AAC TGG GCC AAG GTT TTA ATT GTG TTG CTA CTC TTT GCC GGC GTT GAT GGG	468 507 546 576
	(2) INFORMATION FOR SEQ ID NO:12:	
5	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
10	<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: homosapiens</li><li>(C) INDIVIDUAL ISOLATE: HK3</li></ul>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:	
15	TAT GAA GTG CGC AAC GTG TCC GGG ATA TAC CAT GTC ACG AAC GAC TGC TCC AAC TCA AGC GTC GTG TAT GAG ACA GCA GAC ATG ATC ATG CAT ACC CCT GGA TGC GTG CCC TGC GTA CGG GAG AAC AAC TCC TCC CGC TGT TGG GTA GCG CTC ACT CCC ACG CTC GCG ACG ACC ACG	39 78 117 156 195
20	ACA ATA CGA CGT CAC GTC GAC TTG CTC GTT GGG GCG GCT GCC TTC TGC TCC GCT ATG TAC GTG GGG GAT CTC TGC GGA TCT GTT TTC CTT GTC TCC CAG CTG TTC ACC TTC TCG CCT CGC CGA CAC GAG ACA GTA CAG GAC TGC AAC TGC TCA CTC TAT CCC GGC CAC GTA TCA GGT CAC CGC ATG GCT TGG GAT ATG ATG ATG AAC TGG TCC CCT ACA GCA GCC CTA GTG GTG TCG CAA TTA CTC CGG ATC CCG CAA GCT GTC GTC GTC GTG GCG GGC GCC CAC TGG GGA GTC CTA GCG GGC CTT GCC TAC TAT TCC ATG GTG GGA AAC TGG GCT AAG GTT TTG ATT	234 273 312 351 390 429 468 507 546
	GTG ATG CTA CTT TTT GCC GGC GTT GAT GGG	576
25	(2) INFORMATION FOR SEQ ID NO:13:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
30	<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: homosapiens</li><li>(C) INDIVIDUAL ISOLATE: HK4</li></ul>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:	
35	CAT GAA GTG CAC AAC GTA TCC GGG ATC TAC CAT GTC ACG AAC GAC TGC TCC AAC TCA AGT ATT GTG TAT GAG GCA GCG GAC ATG ATC ATG CAT ACC CCC GGG TGC GTG CCC TGC GTC	39 78 117

35

(vi)

- 58 -

5	CGG GAG AAC AAC TCC TCC CGT TGC TGG GTA GCG CTC ACT CCC ACG CTC GCG GCC AGG AAC GCC AGC ATC CCC ACT ACG ACA ATA CGA CGC CAT GTC GAC TTG CTC GTT GGG GCG GCT GCT TTC TGC TCC GCC ATG TAC GTG GGA GAT CTC TGC GGA TCT GTC GTC GTC TCC CAG TTG TTC ACC TTC TCG CCT CGC CGG CAT GAG ACG GTA CAG GAC TGC AAT TGC TCA ATC CGC CGG CAT GAG ACG GTA CAG GAC TGC AAT TGC TCA ATC TAT CCC GGC CAC GTA TCA GGT CAC CGC ATG GCT TGG GAT ATG ATG ATG ATG AAC TGG TCA CCT ACA GCA GCC CTA GTG GTA TCG CAG TTA CTC CGA CTC CCA CAA GCT GTC ATG GAC ATG GTG GTG GCG GGA GCC CAC TGG GGA GCC CAC TGG GGA GCC CAC TGG GGA GCC CAC AGG GCC CTT GCT TAC TAT TCC ATG GTG GGG AAC TGG GCC AAG GTT TTG ATT GTG ATG CTA CTC TTT GCC GGC GTT GAC GGG	156 195 234 273 312 351 390 429 468 507 546 576
10	(2) INFORMATION FOR SEQ ID NO:14:  (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 576 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
15	(vi) ORIGINAL SOURCE: (A) ORGANISM: homosapiens (C) INDIVIDUAL ISOLATE: HK5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:	
20	TAT GAA GTG CGC AAC GTG TCC GGG GTA TAC CAT GTC ACG AAC GAC TGC TCC AAC TTA AGC ATC GTG TAC GAG ACA ACG GAC ATG ATC ATG CAC ACC CCT GGG TGC GTG CCC TGC GTT CGG GAA AAC AAC TCC TCC CGT TGT TGG GTA GCG CTC GCC CCC ACG CTC GCC AGG AAC GCC AGC GTC CCC ACC ACC ACG GCA ATA CGA CGC CAC GTC GAC TTG CTC GTT GGG GCG GCT GCT TTC TGC TCC GCT ATG TAC GTG GGG GAT CTT TGC GGA TCT GTT GTC GTC GTC GCT GTC GCT GTC GCT GTC GCT GCT	39 78 117 156 195 234 273 312
25	CGC CGA CAC GAG ACG GTA CAG GAC TGC AAC TGC TCA ATC TAT CCC GGC CAC GTA ACA GGT CAC CGC ATG GCT TGG GAT ATG ATG ATG AAC TGG TCA CCT ACA ACA GCC CTA GTG GTG TCG CAG TTA CTC CGG ATC CCG CAA GCT GTC GTG GAC ATG GTA GCG GGG GCC CAC TGG GGG GTC CTG GCG GGC CTT GCC TAC TAT TCC ATG GTG GGA AAC TGG GCT AAG GTT TTG ATT GTG ATG CTA CTT TTT GCC GGC GTT GAT GGG	351 390 429 468 507 546 576
30	(2) INFORMATION FOR SEQ ID NO:15:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	

ORIGINAL SOURCE:

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(A)
                           ORGANISM: homosapiens
                      (C)
                           INDIVIDUAL ISOLATE:
           (xi)
                      SEQUENCE DESCRIPTION: SEO ID NO:15:
     TAT GAA GTG CGC AAC GTG TCC GGG ATA TAC CAT GTC ACG
                                                                   39
      AAC GAC TGC TCC AAC TCA AGC ATC GTG TAT GAA ACA GCG
                                                                   78
     GAC ATG ATT ATG CAT ACC CCT GGA TGC ATG CCC TGC GTT
                                                                  117
 5
      CGG GAG AAC AAC TCC TCC CGT TGC TGG GTG GCG CTC ACT
                                                                  156
     CCC ACG CTC GCG GCT AGG AAT GTC AGC GTC CCC ACT ACG
                                                                  195
     ACA ATA CGA CGC CAC GTC GAC TTG CTC GTT GGG GCG GCT
                                                                  234
     GCT TTC TGC TCC GCT ATG TAC GTG GGG GAT CTC TGC GGA
                                                                  273
     TCT GTT TTC CTC GTC TCC CAG CTG TTC ACC TTT TCG CCT
                                                                  312
     CGC CGA CAC GAG ACG GTA CAG GAC TGC AAC TGC TCA ATC
                                                                  351
     TAT CCC GGC CAC GTA TCA GGT CAC CGC ATG GCT TGG GAT
                                                                 390
10
     ATG ATG AAC TGG TCG CCC ACA ACA GCC CTA GTG GTG
                                                                 429
                                                              468
507
546
576
     TCG CAG TTA CTC CGG ATC CCG CAA GCT ATC GTG GAC ATG
     GTG GCG GGG GCC CAC TGG GGA GTC CTA GCG GGC CTT GCC
     TAC TAT TCC ATG GTG GGC AAC TGG GCT AAG GTT TTG ATT
     GTG ATG CTA CTG TTT GCC GGC GTT GAT GGG
                                                                  576
      (2)
           INFORMATION FOR SEO ID NO:16:
15
           (i)
                      SEQUENCE CHARACTERISTICS:
                      (A)
                          LENGTH: 576 base pairs
                           TYPE: nucleic acid
                      (B)
                           STRANDEDNESS: single
                      (C)
                           TOPOLOGY: linear
                      (D)
20
                      ORIGINAL SOURCE:
           (vi)
                      (A)
                           ORGANISM: homosapiens
                      (C)
                           INDIVIDUAL ISOLATE:
                                                 IND5
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:16:
     TAT GAA GTG CGC AAC GTG TCC GGG GTG TAC CAT GTC ACG
     AAC GAC TGC TCC AAC TCA AGT ATT GTG TAT GAG GCA GCG GAC ATG ATC ATG CAC ACT CCC GGG TGC GTG CCC TGC GTT CGG GAG GGC AAC TCC TCT CGC TGC TGG GTA GCG CTC ACT
                                                                   78
25
                                                                  117
                                                                 156
     CCC ACT CTC GCG GCC AGG AAC GCC AGC GTC TCC ACC ACG
                                                                 195
     ACA ATA CGA CAC CAC GTC GAT TTG CTC GTT GGG GCG GCT
                                                                 234
     GCT TTC TGT TCC GCT ATG TAC GTG GGG GAT CTA TGC GGA
                                                                 273
     TCT GTT TTC CTC GTC TCC CAG CTG TTC ACC TTC TCA CCG
                                                                 312
     CGC CGG CAT GAG ACA GTA CAG GAC TGC AAT TGC TCC ATC
                                                                 351
30
     TAT CCC GGC CAC GTA TCA GGT CAC CGC ATG GCC TGG GAT
                                                                 390
     ATG ATG ATG AAC TGG TCA CCT ACA GCA GCC CTA GTG GTA
                                                                 429
                                                              468
507
546
     TCG CAG TTG CTC CGG ATC CCA CAA GCT GTC GTG GAT ATG
     GTG GCG GGG GCC CAC TGG GGA ATC CTG GCG GGC CTT GCC
     TAC TAT TCC ATG GTA GGG AAC TGG GCT AAG GTT TTG ATT
     GTG ATG CTA CTC TTT GCC GGC GTT GAC GGG
```

<sup>35 (2)</sup> INFORMATION FOR SEQ ID NO:17:

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(i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH: 576 base pairs
                     (B)
                          TYPE: nucleic acid
                     (C)
                          STRANDEDNESS: single
                     (D)
                          TOPOLOGY: linear
           (vi)
                     ORIGINAL SOURCE:
                          ORGANISM: homosapiens
                     (A)
 5
                     (C)
                          INDIVIDUAL ISOLATE:
                     SEQUENCE DESCRIPTION: SEQ ID NO:17:
           (xi)
     TAT GAG GTG CGC AAC GTG TCC GGG GTG TAC CAT GTC ACG
                                                                39
     AAC GAC TGC TCC AAC TCA AGT ATT GTG TAT GAG GCA GCG
                                                                78
     GAC ATG ATC ATG CAC ACC CCC GGG TGC GTG CCC TGC GTT
                                                               117
10
     CGG GAG GGC AAC TTC TCT AGT TGC TGG GTA GCG CTC ACT
                                                               156
     CCC ACT CTC GCG GCT AGG AAC GCC AGC GTC CCC ACC ACG
                                                               195
     ACA ATA CGA CGC CAC GTC GAT TTG CTC GTT GGG GCG GCT
                                                               234
     GCT TTC TGT TCC GCT ATG TAC GTG GGG GAT CTC TGC GGA
                                                               273
     TCT GTT TTC CTT GTC TCC CAG CTG TTC ACC TTC TCA CCG
                                                               312
     CGC CGG CAT GAG ACA GTA CAG GAC TGC AAT TGC TCC ATC
                                                               351
     TAT CCC GGC CAC GTA TCA GGT CAC CGC ATG GCT TGG GAT
                                                               390
     ATG ATG AAC TGG TCA CCT ACA GCG GCC CTA GTG GTA
                                                               429
15
     TCG CAG TTG CTC CGG ATC CCA CAA GCT GTC GTG GAT ATG
     GTG GCG GGG GCC CAC TGG GGA ATC CTG GCG GGC CTT GCC
                                                              507
     TAC TAT TCC ATG GTA GGG AAC TGG GCT AAG GTT TTG ATT
                                                             546
     GTG ATG CTA CTC TTT GCC GGC GTT GAC GGG
                                                               576
          INFORMATION FOR SEO ID NO:18:
      (2)
20
                     SEQUENCE CHARACTERISTICS:
           (i)
                          LENGTH: 576 base pairs
                     (A)
                     (B)
                          TYPE: nucleic acid
                          STRANDEDNESS: single
                     (C)
                          TOPOLOGY: linear
           (vi)
                     ORIGINAL SOURCE:
25
                     (A)
                         ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE: P10
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:18:
     TAT GAA GTG CGC AAC GTG TCC GGG GTG TAC CAT GTC ACG
                                                                39
     AAC GAC TGC TCC AAC TCA AGT ATT GTG TAT GAG GCA GCG
                                                                78
     GAC ATG ATA ATG CAC ACC CCC GGG TGC GTG CCC TGT GTT
30
                                                               117
     CGG GAG AAC AAC TCC TCC CGC TGC TGG GTA GCG CTC ACT
                                                               156
     CCC ACA CTC GCG GCT AGG AAT TCC AGC GTC CCA ACT ACG
                                                               195
     GCA ATA CGA CGC CAT GTC GAT TTG CTC GTT GGG GCG GCT
                                                               234
     GCT TTC TGC TCC GCT ATG TAC GTG GGG GAT CTC TGC GGA
     TCT GTT CTC CTC GTC TCC CAG CTG TTC ACC TTC TCA CCT
     CGC CGG CAT TGG ACA GTA CAG GAC TGC AAT TGT TCA ATC
     TAT CCT GGC CAC GTA TCA GGT CAC CGC ATG GCT TGG GAT
                                                              390
35
     ATG ATG AAC TGG TCG CCC ACA GCA GCC CTA GTG GTG
                                                             429
```

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•	TCG CAG CTA CTC CGG ATC CCA CAA GCT ATC TTG GTG GCG GGC GAC TGG GGA GTC CTG GCG GGC TAC TAT TCC ATG GTG GGG AAC TGG GCT AAG GTC GTG ATG CTA CTC TTT GCC GGC GTT GAC GGA	CTT GCC 507
5	(2) INFORMATION FOR SEQ ID NO:19:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
10	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: homosapiens     (C) INDIVIDUAL ISOLATE: S9</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID	NO:19:
15	TAT GAA GTG CGC AAC GTA TCC GGG GCG TAC CAT AAC GAC TGC TCC AAC TCA AGT ATT GTG TAC GAG GAC GTG ATC ATG CAT ACC CCC GGG TGT GTA CCC CAG GAG GGT AAC TCC TCC CAA TGC TGG GTG GCG CCC ACG CTC GCG GCC AGG AAC GCT ACC GTC CCC ACA ATA CGA CGT CAT GTC GAT TTG CTC GTT GGG GTT TTC TGC TCC GCT ATG TAC GTG GGG GAC CTG	GCA GCG 78 TGC GTT 117 CTC ACC 156 ACC ACG 195 GCG GCT 234
20	TCT GTT TTC CTC ATC TCC CAG CTG TTC ACC ATC CGT CGG CAT GAG ACA GTA CAG AAC TGC AAT TGC TAT CCC GGA CAC GTG ACA GGT CAT CGC ATG GCC ATG ATG ATG ATG ATG AAC TGG TCG CCT ACA ACA GCC CTA TCG CAG CAG CTA CTC CGG ATC CCA CAA GCT GTC ATG GTG GCG GCC CAC TGG GGA GTC CTG GCG GGC TAC TAT TCC ATG GTG GGG AAC TGG GCT AAG GTT GTG ATG ATG CTA CTT TTT GCT GGT GTT GAC GGG	TCG CCC 312 TCA ATC 351 TGG GAT 390 GTG GTA 429 GAT ATG 468 CTC GCC 507
25	(2) INFORMATION FOR SEQ ID NO:20:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
30	<pre>(vi) ORIGINAL SOURCE:</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID	NO:20:
35	TAT GAA GTG CGC AAC GTG TCC GGG GCG TAC CAT AAC GAC TGC TCC AAC TCA AGC ATT GTG TAT GAG GAC GTG ATC CTG CAC ACC CCT GGG TGC GTG CCC	GCA GTG 78

- 62 -

5	CCC ACG CTC GCG GCC ACA ATA CGA CGT CA GCT TTC TGC TCC GCT TCT GTT TTC CTT GTT CGT CGG CAT GAG ACC TAT CCC GGC CAC GTC ATG ATG ATG AAC TGC GTG GCG GGG GCC CAC GTG GCG GGG GCC CAC TAC TAT TCC ATG GTC	C AGG AAC TCC AGC GTC CCC ACT ACG C GTC GAT TTG CTC GTT GGG GCG GCT T ATG TAC GTG GGG GAT CTC TGC GGA T TCC CAG CTG TTC ACC TTC TCG CCT A GTA CAG GAC TGC AAC TGT TCA ATC A ACA GGT CAC CGC ATG GCT TGG GAT G TCG CCT ACA GCA GCC TTA GTG GTA G ATC CCA CAA GCT GTC GTG GAC ATG C TGG GGA GTC CTG GCG GGC CTT GCC G GGG AAC TGG GCT AAG GTT CTG ATT	156 195 234 273 312 351 390 429 468 507 546
	GTG ATG CTA CTC TT	T GCC GGC GTT GAC GGG	576
10	(2) INFORMATION FO	OR SEQ ID NO:21:	
	(A) (B) (C)	TYPE: nucleic acid STRANDEDNESS: single	
	(D)	TOPOLOGY: linear	
15	(vi) ORIC (A) (C)		
	(xi) SEQU	UENCE DESCRIPTION: SEQ ID NO:21:	
20	AAC GAC TGC TCC AAC GAC ATG ATC ATG CAC CGG GAG AAC AAC TCC CCC ACG CTC GCG GCC	C ACC CCC GGG TGC GTG CCC TGC GTT C TCC CGC TGC TGG GTA GCG CTC ACT C AGG AAC TCC AGC GTC CCC ACT ACG	39 78 117 156 195 234
		C ATG TAC GTG GGG GAC CTC TGC GGA	273 312
05			351 390
25	ATG ATG ATG AAC TGG TCG CAG TTA CTC CGG GTG GCG GGG GCC CAC TAC TAT TCC ATG GTG	G TCA CCT ACA ACA GCT CTA GTA GTA G ATC CCA CAA GCT ATC GTG GAC ATG C TGG GGA GTC CTA GCG GGC CTT GCC G GGG AAC TGG GCT AAG GTT TTG ATT	429 468 507 546
	GII AIG CIA CIC III	GCC GGC GII GAC GGG	576
30	(2) INFORMATION FO	OR SEQ ID NO:22:	
	(A)	JENCE CHARACTERISTICS:  LENGTH: 576 base pairs  TYPE: nucleic acid  STRANDEDNESS: single  TOPOLOGY: linear	
35	(vi) ORIG	GINAL SOURCE:	

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```
(A)
                            ORGANISM: homosapiens
                       (C)
                            INDIVIDUAL ISOLATE:
            (xi)
                       SEQUENCE DESCRIPTION: SEQ ID NO:22:
      TAT GAA GTG CGC AAC GTG TCC GGG GTG TAT CAT GTC ACG
                                                                    39
      AAC GAC TGT TCC AAC TCA AGC ATT GTG TAT GAG ACA GCG
                                                                    78
      GAC ATG ATC ATG CAT ACC CCC GGG TGC GTG CCC TGC GTT CGG GAG GCC AAC TCC TCC CGC TGC TGG GTA GCG CTC ACT CCC ACG CTA GCA GCC AGG AAC ACC AGC GTC CCC ACT ACG
                                                                    117
                                                                   156
                                                                   195
      ACA ATA CGA CGC CAC GTC GAT TTG CTC GTT GGG GCG GCT
                                                                   234
      GCT TTC TGC TCC GTT ATG TAC GTG GGG GAT CTC TGC GGA
                                                                   273
      TCT GTT TTC CTC GTC TCC CAG CTG TTC ACT TTT TCA CCT
                                                                   312
      CGC CGG CAC GAG ACA GTA CAG GAC TGC AAC TGT TCC ATC
                                                                   351
      TAT CCC GGC CAC GTA TCA GGT CAC CGC ATG GCT TGG GAC
                                                                   390
      ATG ATG AAC TGG TCA CCT ACA GCA GCC CTG GTG GTA
10
                                                                   429
      TCG CAG TTA CTC CGG ATC CCA CAA GCT GTC GTG GAC ATG
                                                                   468
      GTA GCG GGG GCC CAC TGG GGA GTC CTG GCG GGC CTT GCA
                                                                   507
      TAC TAT TCC ATG GTG GGG AAC TGG GCT AAG GTT TTG ATT
                                                                   546
      GTG ATG CTA CTC TTT GCT GGC GTT GAC GGG
                                                                   576
      (2)
           INFORMATION FOR SEO ID NO:23:
15
                      SEQUENCE CHARACTERISTICS:
            (i)
                            LENGTH: 576 base pairs
                       (A)
                            TYPE: nucleic acid
                       (B)
                       (C)
                            STRANDEDNESS: single
                       (D)
                            TOPOLOGY: linear
20
           (vi)
                      ORIGINAL SOURCE:
                       (A)
                            ORGANISM: homosapiens
                      (C)
                            INDIVIDUAL ISOLATE: T3
                      SEQUENCE DESCRIPTION: SEQ ID NO:23:
           (xi)
      TAC GAA GTG CGC AAC GTG TCC GGG GTG TAC TAT GTC ACG
      AAC GAC TGT TCC AAC TCA AGC ATT GTG TAT GAG ACA GCG
                                                                   78
25
      GAC ATG ATC ATG CAC ACC CCT GGG TGC GTG CCC TGC GTT
                                                                   117
      CGG GAG AGC AAT TCC TCC CGC TGC TGG GTA GCG CTT ACT
                                                                   156
      CCC ACG CTC GCG GCC AGG AAC GCC AGC GTC CCC ACT AAG
                                                                   195
      ACA ATA CGA CGT CAC GTC GAC TTG CTC GTT GGG GCG GCT
                                                                   234
      GCT TTC TGT TCC GCT ATG TAC GTG GGG GAT CTC TGC GGA
                                                                   273
      TCT GTT TTC CTC GTC TCC CAG CTG TTC ACT TTC TCG CCT
                                                                   312
      CGC CGG CAT GAG ACA GTA CAG GAC TGC AAC TGC TCA ATC
                                                                   351
      TAT CCC GGC CAC GTA ACA GGT CAC CGT ATG GCT TGG GAT
30
                                                                   390
      ATG ATG ATG AAC TGG TCG CCC ACA ACG GCA CTA GTG GTG
                                                                   429
      TCG CAG TTG CTC CGG ATC CCA CAA GCT GTC GTG GAC ATG
                                                                   468
      GTG GCG GGG GCC CAC TGG GGA GTC CTG GCG GGC CTT GCC
                                                                   507
      TAC TAT TCC ATG GTG GGG AAC TGG GCT AAG GTT TTG ATT
                                                                   546
      GTG CTG CTA CTC TTT GCC GGC GTT GAT GGG
                                                                   576
35
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<sup>(2)</sup> INFORMATION FOR SEQ ID NO:24:

PCT/US94/07320 WO 95/01442

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•	( <i>)</i> (E (C	QUENCE CHARACTERISTICS:  A) LENGTH: 576 base pairs B) TYPE: nucleic acid C) STRANDEDNESS: single D) TOPOLOGY: linear
5	(2	IGINAL SOURCE:  L) ORGANISM: homosapiens  C) INDIVIDUAL ISOLATE: T10
	(xi) SE	QUENCE DESCRIPTION: SEQ ID NO:24:
10	AAC GAC TGC TCC AGAC TTG ATC ATG CGG GAG GGC AAC TCCC ACG CTC GCG GACG ATA CGA CGC CGC TTC TGC TCC GGC	AC GTG TCC GGG ATG TAC CAT GTC ACG  AC TCA AGC ATT GTG TTT GAG GCA GCG  AC ACC CCC GGG TGC GTG CCC TGC GTT  CCC TCC CGC TGC TGG GTA GCG CTC ACT  ACC AGG AAC ACC AGC GTC CCC ACT ACG  ATT GTC GAT TTG CTC GTT GGG GCG GCT  ACT ATG TAT GTG GGA GAC CTC TGC GGA  ACT ATG TAT GTG GGA GAC CTC TCC GCT  ACT TCC TCC CAG CTG TTC ACC TTC TCC CCT  ACT ATG TAT GTG GGA GAC CTC TCC CCT  ACT ACG CTG TTC ACC TTC TCC CCT  ACC ACG ACC ACC ACC ACC ACC ACC ACC ACC
15	CGC CGG CAT GAG A TAT CCC GGC CAT C ATG ATG ATG AAC T TCG CAG TTA CTC C GTG ACA GGG GCC C TAC TAT TCC ATG G	CT TTG CAG GAC TGC AAC TGC TCA ATC TG TCA GGT CAC CGC ATG GCT TGG GAC GG TCG CCT ACA ACA GCT CTA GTG GTG GG ATC CCA CAA GCT GTC ATG GAC ATG AC TGG GGA GTC CTG GCG GGC CTT GCC GCG GGG AAC TGG GCT AAG GTT TTA ATT TGCC GGC GTT GAT GGG 576
20	(i) SE	FOR SEQ ID NO:25: QUENCE CHARACTERISTICS: DENGTH: 576 base pairs
	(B	) TYPE: nucleic acid ) STRANDEDNESS: single
25	• •	IGINAL SOURCE: ) ORGANISM: homosapiens ) INDIVIDUAL ISOLATE: US6
	(xi) SE	QUENCE DESCRIPTION: SEQ ID NO:25:
30	AAC GAC TGC TCC A GAC ATG ATC ATG C CGG GAG AAC AAT T CCC ACG CTC GCG G ACA ATA CGA CGC C ACT TTC TGC TCC G TCC GTT TTC CTC A	AC GTG TCC GGG ATG TAC CAT GTC ACG  AC TCA AGC ATT GTG TAT GAG GCA GCG  AC ACT CCC GGG TGC GTG CCC TGT GTT  CC TCC CGC TGC TGG GTA GCG CTC ACT  CC AGG AAC GCT AGC GTC CCC ACT ACG  AC GTC GAT TTG CTC GTT GGG GCG GCT  AC ATG TAC GTG GGG GAC CTC TGC GGG  TC TCC CAG CTG TTC ACC TTC TCG CCT  39  39  39  30  31  31  31  31  31  31  31  31  31
35	TAT CCC GGC CAC G	CA GTA CAG GAC TGC AAT TGT TCA ATC 351 TA TCA GGT CAC CGC ATG GCT TGG GAT 390 GG TCA CCT ACA GCA GCC CTA GTG GTA 429

- 65 -

o	TCG CAG TTA CTC CGG ATC CCA CAA GCT GTC ATG GAC ATG GTG GCG GGG GCC CAC TGG GGA GTC CTG GCG GGC CTT GCC TAC TAT TCC ATG GTG GGG AAC TGG GCT AAG GTT CTG ATT GTG TTG CTA CTC TTT GCC GGC GTT GAC GGG	468 507 546 576
5	(2) INFORMATION FOR SEQ ID NO:26:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single	
10	(D) TOPOLOGY: linear  (vi) ORIGINAL SOURCE:  (A) ORGANISM: homosapiens  (C) INDIVIDUAL ISOLATE: T2	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:	
15	GCC CAA GTG AGG AAC ACC AGC CGC GGT TAC ATG GTG ACT AAC GAC TGT TCC AAT GAG AGC ATC ACC TGG CAG CTC CAA GCC GCG GTT CTC CAC GTC CCC GGG TGT ATC CCG TGT GAG AGG CTG GGA AAT ACA TCC CGA TGC TGG ATA CCG GTC ACA CCA AAC GTG GCC GTG CGG CAG CCC GGC GCT CTT ACG CAG	39 78 117 156 195
20	GGC TTG CGG ACG CAC ATC GAC ATG GTT GTG ATG TCC GCC ACG CTC TGC TCT GCC CTC TAC GTG GGG GAC CTC TGC GGC GGG GTG ATG CTC GCA GCC CAG ATG TTC ATT GTC TCG CCG CGA CGC CAC TGG TTT GTG CAA GAA TGC AAT TGC TCC ATC TAC CCC GGT ACC ATC ACT GGA CAC CGT ATG GCA TGG GAC ATG ATG ATG AAC TGG TCG CCC ACA GCC ACC ATG ATC CTG GCG TAC GCG ATG CGC GTT CCC GAG GTC ATC ATA GAC ATC ATC GGC GGG GCT CAC TGG GGC GTC ATG TTT GGC TTG GCC TAC TTC TCT ATG CAG GGA GCG TGG GCG AAG GTC ATT GTC ATC CTC TTG CTG GCT GCT GGG GTG GAC GCG	234 273 312 351 390 429 468 507 546 576
25	(2) INFORMATION FOR SEQ ID NO:27:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
30	<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: homosapiens</li><li>(C) INDIVIDUAL ISOLATE: T4</li></ul>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:	
35	GCA CAA GTG AAG AAC ACC ACT AAC AGC TAC ATG GTG ACC AAC GAC TGT TCT AAT GAC AGC ATC ACT TGG CAG CTC CAG GCC GCG GTC CTC CAC GTC CCC GGG TGT GTC CCG TGC GAG	39 78 117

- 66 -

5	CCA AAC GTG GCC GTG GGC TTG CGG ACG CAC ACG CTC TGC TCT GCT GGG GTG ATG CTC GCA CAA CAT CAC TGG TTT TAC CCT GGC ACC ATC ATG ATG ATG AAC TGG GCG TAC GCG ATG CGC GTT AGC GGG GCA CAC TAC TTC TCT ATG CAG	A TCT CGG TGC TGG ATA CCG GTT TCA G CGG CAG CCC GGC GCC CTC ACG CAG C ATT GAC ATG GTT GTG ATG TCC GCC T CTT TAC GTG GGG GAC CTC TGC GGC A GCC CAG ATG TTC ATC GTC TCG CCG T GTG CAA GAC TGC AAT TGC TCT ATC C ACT GGA CAC CGT ATG GCA TGG GAT G TCG CCC ACG GCC ACC ATG ATC CTG C GTT CCC GAG GTC ATC TTA GAC ATC C TGG GGC GTC ATG TTC GGC TTG GCC G GGA GCG TGG GCG AAA GTC GTT GTC C GCT GGG GTG GAC GCG C GCT GGG GTG GAC GCG	156 195 234 273 312 351 390 429 468 507 546 576
10	(i) SEQU (A) (B)	DR SEQ ID NO:28:  JENCE CHARACTERISTICS:  LENGTH: 576 base pairs  TYPE: nucleic acid  STRANDEDNESS: single  TOPOLOGY: linear	
15	(A) (C)	FINAL SOURCE: ORGANISM: homosapiens INDIVIDUAL ISOLATE: T9 UENCE DESCRIPTION: SEQ ID NO:28:	
20	AAT GAC TGT TCC AAC GCC GCG GTC CTC CAC AGA GTT GGA AAC GCG CCA AAC GTA GCT GTG GGC TTG CGG ACG CAC ACG CTC TGC TCC GCT GGG GTA ATG CTC GCC	ACC AGT ACC AGC TAC ATG GTG ACA GAC AGC ATC ACC TGG CAA CTC CAG GTC CCC GGG TGC GTC CCG TGC GAG TCG CGG TGC TGG ATA CCG GTC TCG CAG CGG CCT GGC GCC CTC ACG CAG ATC GAC ATG GTT GTG ATG TCC GCC CTC TAC GTG GGG GAT CTC TGC GGC GCT CAG ATG TTC ATT ATC TCG CCG GTG CAG GAA TGC AAC TGC TCC ATT	39 78 117 156 195 234 273 312 351
25	TAC CCT GGT ACC ATC ATG ATG ATG AAC TGG GCG TAC GCG ATG CGC ATC AGC GGA GCT CAC TAC TTC TCT ATG CAG	ACT GGA CAC CGT ATG GCA TGG GAC TCG CCC ACA ACC ACC ATG ATC TTG GTT CCC GAG GTC ATC ATA GAC ATC TGG GGC GTC ATG TTC GGC CTA GCC GGA GCG TGG GCG AAG GTC GTT GTC GCT GGC GTG GAC GCG	390 429 468 507 546 576
30	(i) SEQU (A) (B)	R SEQ ID NO:29:  ENCE CHARACTERISTICS:  LENGTH: 576 base pairs  TYPE: nucleic acid	

- STRANDEDNESS: single TOPOLOGY: linear
- (C) (D)

35 (vi) ORIGINAL SOURCE:

- 67 -

```
0
                           ORGANISM: homosapiens
                      (A)
                           INDIVIDUAL ISOLATE:
                      (C)
           (xi)
                     SEQUENCE DESCRIPTION: SEO ID NO:29:
     GTC CAA GTG AAA AAC ACC AGT ACC AGC TAT ATG GTG ACC
                                                                 39
     AAT GAC TGC TCC AAC GAC AGC ATC ACT TGG CAA CTT GAG
                                                                  78
     GCT GCG GTC CTC CAC GTT CCC GGG TGT GTC CCG TGC GAG
                                                                 117
 5
     AAA GTG GGA AAT ACA TCT CGG TGC TGG ATA CCG GTC TCA
                                                                 156
     CCA AAT GTG GCC GTG CAG CGG CCT GGC GCC CTC ACG CAG
                                                                 195
     GGC TTG CGG ACT CAC ATC GAC ATG GTC GTG ATG TCC GCC
                                                                234
     ACG CTC TGC TCC GCT CTT TAC GTG GGG GAC TTC TGC GGT
                                                                273
     GGG ATG ATG CTC GCA GCC CAA ATG TTC ATT GTC TCG CCG CGC CAC CAC TCG TTT GTG CAG GAA TGC AAC TGC TCC ATC
                                                                312
                                                                351
     TAC CCC GGT ACC ATC ACC GGG CAC CGT ATG GCA TGG GAC
                                                                390
                                                             445
468
507
546
576
10
     ATG ATG ATG AAC TGG TCG CCC ACG GCC ACT TTG ATC CTG
     GCG TAC GTG ATG CGC GTT CCC GAG GTC ATC ATA GAC ATC
     ATT AGC GGG GCG CAT TGG GGC GTC TTG TTC GGC TTA GCC
     TAC TTC TCT ATG CAG GGA GCG TGG GCG AAA GTC GTT GTC
     ATC CTT CTG CTA GCC GCT GGG GTG GAC GCG
          INFORMATION FOR SEQ ID NO:30:
     (2)
15
                     SEQUENCE CHARACTERISTICS:
           (i)
                          LENGTH: 576 base pairs
                     (A)
                      (B)
                           TYPE: nucleic acid
                      (C)
                           STRANDEDNESS: single
                     (D)
                          TOPOLOGY: linear
20
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                           INDIVIDUAL ISOLATE: DK8
                     (C)
                     SEQUENCE DESCRIPTION: SEQ ID NO:30:
           (xi)
     GTG GAA GTC AGG AAC ATC AGT TCC AGC TAC TAC GCC ACC
                                                                 39
78
     AAT GAT TGC TCA AAC AAC AGC ATC ACC TGG CAA CTC ACC
25
     GAC GCA GTT CTC CAC CTT CCC GGA TGC GTC CCA TGT GAG
                                                                 117
     AAT GAC AAT GGC ACC CTG CGC TGC TGG ATA CAA GTG ACA
                                                                 156
     CCT AAT GTG GCT GTG AAA CAC CGC GGC GCA CTT ACT CAT
                                                                 195
     AAC CTG CGA ACA CAC GTC GAC GTG ATC GTA ATG GCA GCT
                                                                234
     ACG GTC TGC TCG GCC TTG TAT GTG GGA GAC GTA TGC GGG
                                                                273
     GCC GTG ATG ATC GTG TCG CAG GCT CTC ATA ATA TCG CCT
                                                                312
     GAA CGC CAC AAC TTT ACC CAG GAG TGC AAC TGT TCC ATC
                                                                351
     TAC CAA GGT CAT ATC ACC GGC CAC CGC ATG GCA TGG GAC
                                                                390
30
     ATG ATG CTA AAC TGG TCA CCA ACT CTT ACC ATG ATC CTC
                                                                429
                                                             50.
546
57€
     GCC TAT GCC GCT CGT GTT CCT GAG CTA GCC CTC CAG GTT
     GTC TTC GGC GGC CAT TGG GGC GTG GTG TTT GGC TTG GCC
     TAT TTC TCC ATG CAG GGA GCG TGG GCC AAA GTC ATT GCC
     ATC CTC CTT CTT GTC GCA GGA GTG GAT GCA
35
     (2) INFORMATION FOR SEQ ID NO:31:
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```
(i)
                     SEQUENCE CHARACTERISTICS:
                          LENGTH: 576 base pairs
                      (A)
                      (B)
                          TYPE: nucleic acid
                          STRANDEDNESS: single
                      (C)
                          TOPOLOGY: linear
                      (D)
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
 5
                     (C)
                          INDIVIDUAL ISOLATE: DK11
           (xi)
                     SEQUENCE DESCRIPTION: SEO ID NO:31:
      GTG GAA GTC AGG AAC ACC AGT TCT AGT TAC TAC GCC ACC
                                                                 39
      AAT GAT TGC TCA AAC AAC AGC ATC ACC TGG CAA CTC ACC
                                                                78
      AAC GCA GTT CTC CAC CTT CCC GGA TGC GTC CCA TGT GAG
10
      AAT GAC AAT GGC ACC CTG CAC TGC TGG ATA CAA GTG ACA
      CCT AAT GTG GCT GTG AAA CAC CGC GGC GCA CTC ACT CAC
                                                               195
      AAC CTG CGA GCA CAT ATA GAT ATG ATT GTA ATG GCA GCT
                                                               234
      ACG GTC TGC TCG GCC TTG TAT GTG GGA GAC GTG TGC GGG
                                                               273
      GCC GTG ATG ATC GTG TCG CAG GCT TTC ATA GTA TCG CCA
                                                               312
      GAA CAC CAC CAC TIT ACC CAA GAG TGC AAC TGT TCC ATC
                                                               351
      TAC CAA GGT CAC ATC ACC GGC CAC CGC ATG GCA TGG GAC
                                                               390
      ATG ATG CTT AAC TGG TCA CCA ACT CTC ACC ATG ATC CTC
                                                               429
15
      GCC TAT GCC GCC CGT GTT CCT GAG CTA GTC CTT GAA GTC
                                                               468
     GTC TTC GGT GGT CAT TGG GGT GTG GTG TTT GGC TTG GCC
                                                               507
      TAT TTC TCC ATG CAG GGA GCG TGG GCC AAG GTC ATT GCC
                                                               546
      ATC CTC CTT CTT GTA GCA GGA GTG GAT GCA
                                                               576
      (2)
           INFORMATION FOR SEQ ID NO:32:
20
           (i)
                     SEQUENCE CHARACTERISTICS:
                          LENGTH: 576 base pairs
                     (B)
                          TYPE: nucleic acid
                     (C)
                          STRANDEDNESS: single
                     (D)
                          TOPOLOGY: linear
                     ORIGINAL SOURCE:
           (vi)
25
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE: SW3
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:32:
     GTG GAA GTC AGG AAC ATC AGT TCT AGC TAC TAT GCC ACC
                                                                39
     AAT GAT TGC TCA AAC AGC AGC ATC ACC TGG CAA CTC ACC
                                                                78
     AAC GCA GTC CTC CAC CTT CCC GGA TGC GTC CCG TGT GAG
30
                                                               117
     AAT GAT AAT GGC ACC CTG CAC TGC TGG ATA CAA GTG ACA
                                                               156
     CCT AAT GTG GCT GTG AAA CAC CGC GGC GCG CTC ACT CAC
                                                               195
     AAC CTG CGA GCA CAC GTC GAT ATG ATC GTA ATG GCA GCT
                                                               234
     ACG GTC TGC TCG GCC TTG TAT GTG GGA GAC ATG TGC GGG
                                                               273
     GCC GTG ATG ATC GTG TCG CAG GCT TTC ATA ATA TCG CCA
                                                               312
     GAA CGC CAC AAC TTT ACC CAA GAG TGC AAC TGT TCC ATC
                                                               351
     TAC CAA GGT CGT ATC ACC GGC CAC CGC ATG GCG TGG GAC
                                                               390
35
     ATG ATG CTA AAC TGG TCA CCA ACT CTT ACC ATG ATC CTT
                                                               429
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o	GCC TAT GCC GCT CGT GTT CCT GAG CTA GTC CTT GAA GTT GTC TTC GGC GGC CAT TGG GGC GTG GTG TTT GGC TTG GCC TAT TTC TCC ATG CAA GGA GCG TGG GCC AAG GTC ATT GCC ATC CTC CTG CTT GTC GCA GGA GTG GAT GCA	468 507 546 576			
	(2) INFORMATION FOR SEQ ID NO:33:				
5	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear				
10	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: homosapiens     (C) INDIVIDUAL ISOLATE: T8</pre>				
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:				
15	GTG GAA GTT AGA AAC ACC AGT TTT AGC TAC TAC GCC ACC AAT GAT TGC TCG AAC AAC AGC ATC ACC TGG CAG CTC ACC AAC GCA GTT CTC CAC CTT CCC GGA TGC GTC CCA TGT GAG AAT GAC AAT GGC ACC TTG CGC TGC TGG ATA CAA GTA ACA CCT AAT GTG GCT GTG AAA CAC CGT GGC GCA CTC ACT CAC AAC CTG CGA ACG CAT GTC GAC GTG ATC GTA ATG GCA GCT	39 78 117 156 195 234			
20	ACG GTC TGC TCG GCC TTG TAT GTG GGG GAC GTG TGC GGG GCC GTG ATG ATA GCG TCG CAG GCT TTC ATA ATA TCG CCA GAA CGC CAC AAC TTC ACC CAG GAG TGC AAC TGT TCC ATC TAC CAA GGT CAT ATC ACC GGC CAC CGC ATG GCA TGG GAC ATG ATG CTG AAC TGG TCA CCA ACT CTC ACC ATG ATC CTC GCC TAC GCT GCT CGT GTG CCT GAA CTA GTC CTT GAA GTT GTC TTC GGC GGC CAT TGG GGC GTG GTG TTT GGC TTG GCC TAT TTC TCC ATG CAA GGA GCG TGG GCC AAA GTC ATC GCC ATC CTC CTC CTT GTC GCA GGA GTG GAC GCA	273 312 351 390 429 468 507 546 576			
25	(2) INFORMATION FOR SEQ ID NO:34:				
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	·			
30	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: homosapiens     (C) INDIVIDUAL ISOLATE: S83</pre>				
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:				
35	GTG GAG GTC AAG GAC ACC GGC GAC TCC TAC ATG CCG ACC AAC GAT TGC TCC AAC TCT AGT ATC GTT TGG CAG CTT GAA GGA GCA GTG CTT CAT ACT CCT GGA TGC GTC CCT TGT GAG	39 78 117			

- 70 -

o	CGT ACC GCC AAC GTC TCT CGA TGT TGG GTG CCG GTT GCC CCC AAT CTC GCC ATA AGT CAA CCT GGC GCT CTC ACT AAG GGC CTG CGA GCA CAC ATC GAT ATC ATC GTG ATG TCT GCT ACG GTC TGT TCT GCC CTT TAT GTG GGG GAC GTG TGT GGC GCG CTG ATG CTG GCC GCT CAG GTC GTC GTC GTG TCG CCA CAA CAC CAT ACG TTT GTC CAG GAA TGC AAC TGT TCC ATA TAC CCG GGC CGC ATT ACG GGA CAC CGC ATG GCT TGG GAT	156 195 234 273 312 351 390
5	ATG ATG AAC TGG TCG CCC ACT ACC ACC ATG CTC CTG GCG TAC TTG GTG CGC ATC CCG GAA GTC ATC TTG GAT ATT GTT ACA GGA GGT CAT TGG GGT GTA ATG TTT GGC CTC GCT TAC TTC TCC ATG CAG GGA TCG TGG GCG AAG GTC ATC GTT ATC CTC CTG CTG ACT GCT GGG GTG GAG GCG	429 468 507 546 576
10	(2) INFORMATION FOR SEQ ID NO:35:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
15	(vi) ORIGINAL SOURCE:  (A) ORGANISM: homosapiens (C) INDIVIDUAL ISOLATE: DK12  (xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:	20
20	TTA GAG TGG CGG AAT GTG TCC GGC CTC TAC GTC CTT ACC AAC GAC TGT TCC AAT AGC AGT ATC GTG TAT GAG GCC GAT GAC GTC ATT CTG CAC ACA CCT GGC TGT GTA CCT TGT GTT CAG GAC GGC AAT ACA TCT ACG TGC TGG ACC TCA GTG ACG CCT ACA GTG GCA GTC AGG TAC GTC GGA GCA ACC ACC GCT TCG ATA CGC AGT CAT GTG GAC CTG CTA GTG GGC GCC ACG ATG TGC TCT GCG CTC TAC GTG GGT GAT GTG TGT GGG GCC GTC TTC CTT GTG GGA CAA GCC TTC ACG TTC AGA CCT CGT CGC CAT CAA ACA GTC CAG ACC TGT AAC TGC TCG CTG TAC CCA GGC CAT CTT TCA GGA CAT CGA ATG GCT TGG GAT	39 78 117 156 195 234 273 312 351
25	ATG ATG ATG AAT TGG TCC CCC GCT GTG GGT ATG GTG GTA GCG CAC GTC CTG CGT CTG CCC CAG ACC TTG TTC GAC ATA ATA GCT GGG GCC CAT TGG GGC ATC ATG GCG GGC CTA GCC TAT TAC TCC ATG CAG GGC AAC TGG GCC AAG GTC GCT ATC ATG ATG GTT ATG TTT TCA GGA GTC GAT GCC	390 429 468 507 546 576
30	(2) INFORMATION FOR SEQ ID NO:36:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	

ORIGINAL SOURCE:

35

(vi)

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```
(A)
                           ORGANISM:
                                      homosapiens
                      (C)
                           INDIVIDUAL ISOLATE: HK10
            (xi)
                      SEQUENCE DESCRIPTION: SEQ ID NO:36:
      CTA GAG TGG CGG AAT GTG TCT GGC CTC TAT GTC CTT ACC
                                                                  39
      AAC GAC TGT CCC AAT AGC AGT ATT GTG TAT GAG GCC GAT
                                                                  78
      GAC GTC ATT CTG CAC ACA CCT GGC TGT GTA CCT TGT GTT
 5
                                                                 117
      CAG GAC GGC AAT ACA TCC ACG TGC TGG ACC TCG GTG ACA
                                                                 156
      CCT ACA GTG GCA GTC AGG TAC GTC GGA GCA ACC ACC GCC
                                                                 195
      TCG ATA CGC AGT CAT GTG GAC CTG TTA GTG GGC GCG GCC
                                                                 234
      ACG ATG TGC TCT GCG CTC TAC GTG GGC GAT ATG TGT GGG
                                                                273
                                                              312
351
390
429
468
507
546
      GCC GTC TTC CTC GTG GGA CAA GCC TTC ACG TTC AGA CCG
      CGT CGC CAT CAA ACG GTC CAG ACC TGT AAC TGC TCG CTG
      TAC CCA GGC CAC CTT TCA GGA CAT CGA ATG GCT TGG GAT
10
      ATG ATG ATG AAT TGG TCC CCC GCC GTG GGT ATG GTG GTG
      GCG CAC GTC CTG CGG TTG CCC CAG ACC TTG TTC GAC ATA
      ATA GCC GGG GCC CAT TGG GGC ATC TTG GCA GGC CTA GCC
      TAT TAC TCC ATG CAG GGC AAC TGG GCC AAG GTC GCT ATC
      ATC ATG GTT ATG TTT TCA GGG GTC GAT GCC
                                                                576
      (2)
           INFORMATION FOR SEQ ID NO:37:
15
                     SEQUENCE CHARACTERISTICS:
           (i)
                      (A)
                          LENGTH: 576 base pairs
                      (B)
                           TYPE: nucleic acid
                           STRANDEDNESS: single
                      (C)
                      (D)
                           TOPOLOGY: linear
20
           (vi)
                     ORIGINAL SOURCE:
                      (A)
                           ORGANISM: homosapiens
                      (C)
                           INDIVIDUAL ISOLATE: $2
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:37:
     CTA GAG TGG CGG AAT ACG TCT GGC CTC TAT GTC CTC ACC
                                                                  39
     AAC GAC TGT TCC AAT AGC AGT ATT GTG TAT GAG GCC GAT
                                                                  78
25
     GAC GTT ATT CTG CAC ACA CCT GGC TGT GTA CCT TGT GTT
                                                                 117
     CAG GAC GGT AAT ACA TCC ACG TGC TGG ACC CCA GTG ACA
                                                                 156
     CCT ACA GTG GCA GTC AGG TAT GTC GGA GCA ACC ACC GCT
                                                                 195
     TCG ATA CGC AGT CAT GTG GAC CTA TTG GTG GGC GCG GCC
                                                                 234
     ACT ATG TGC TCT GCG CTC TAC GTG GGT GAT ATG TGT GGG
                                                                 273
     GCC GTC TTT CTC GTG GGA CAA GCC TTC ACG TTC AGA CCT CGT CGC CAT CAA ACG GTC CAG ACC TGT AAC TGC TCG CTG
                                                                 312
                                                                 351
30
     TAC CCA GGC CAT CTT TCA GGA CAT CGC ATG GCT TGG GAT
     ATG ATG ATG AAT TGG TCC CCC GCT GTG GGT ATG GTG GTG
     GCG CAC GTT CTG CGT TTG CCC CAG ACC GTG TTC GAC ATA
                                                               468
     ATA GCC GGG GCC CAT TGG GGC ATC TTG GCG GGC CTA GCC
     TAT TAC TCC ATG CAA GGC AAC TGG GCC AAG GTC GCT ATC
                                                               546
     ATC ATG GTT ATG TTT TCA GGG GTC GAC GCC
                                                                 576
35
      (2) INFORMATION FOR SEQ ID NO:38:
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o	(A) (B)	ENCE CHARACTERISTICS: LENGTH: 576 base pairs TYPE: nucleic acid STRANDEDNESS: single TOPOLOGY: linear										
5	(A) (C)	INDIVIDUAL ISOLATE: S52										
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:											
10	AAC GAC TGT TCC AAT GAC GTC ATT CTG CAC CAG GAC GGC AAT ACA CCT ACG GTG GCA GTC TCG ATA CGC AGT CAT ACG CTG TGC TCT GCG GCC GTC TTT CTC GTG	TCC ATG TGC TGG ACC CCA GTG ACA AGG TAC GTC GGA GCA ACC ACC GCT GTG GAC CTA TTA GTG GGC GCC CTC TAT GTG GGT GAT ATG TGT GGG GGA CAA GCC TTC ACG TTC AGA CCT	39 78 117 156 195 234 273 312									
15	TAC CCA GGC CAT GTT ATG ATG ATG AAT TGG GCG CAC ATC CTG CGA CTG GCC GGG GCC CAT	TCA GGA CAT CGA ATG GCT TGG GAT TCC CCC GCT GTG GGT ATG GTG GTG TTG CCC CAG ACC TTG TTT GAC ATA TGG GGC ATC TTG GCG GGC CTA GCC GGC AAC TGG GCC AAG GTC GCT ATT	351 390 429 468 507 546 576									
20	(2) INFORMATION FOR SEQ ID NO:39:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear											
25	(vi) ORIG: (A) (C)											
	(xi) SEQUI	ENCE DESCRIPTION: SEQ ID NO:39:										
30	AAC GAC TGT TCC AAT GAC GTC ATT CTG CAC CAG GAC GGC AAT ACA CCT ACG GTG GCA GTC TCG ATA CGC AGT CAT ACG CTG TGC TCT GCG GCC GTC TTT CTC GTG	TCC ACG TGC TGG ACC CCA GTG ACA AGG TAC GTC GGA GCA ACC ACC GCT GTG GAC CTA TTA GTG GGC GCG GCC CTC TAT GTG GGT GAT ATG TGT GGG GGA CAA GCC TTC ACG TTC AGA CCT	39 78 117 156 195 234 273 312 351									
35	TAC CCA GGC CAT CTT	TCA GGA CAT CGA ATG GCT TGG GAT	390 429									

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o	GCG CAC ATC CTG CGA TTG CCC CAG ACC TTG TTT GAC ATA CTG GCC GGG GCC CAT TGG GGC ATC TTG GCG GGC CTA GCC TAT TAT TCT ATG CAG GGC AAC TGG GCC AAG GTC GCT ATC ATG ATG ATT ATG TTT TCA GGG GTC GAT GCC	468 507 546 576								
5	(2) INFORMATION FOR SEQ ID NO:40:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear									
10	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: homosapiens     (C) INDIVIDUAL ISOLATE: Z4</pre>									
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:									
15	GAG CAC TAC CGG AAT GCT TCG GGC ATC TAT CAC ATC ACC AAT GAT TGT CCG AAT TCC AGT ATA GTC TAT GAA GCT GAC CAT CAC ATC CTA CAC TTG CCG GGG TGC GTA CCC TGT GTG ATG ACT GGG AAC ACA TCG CGT TGC TGG ACG CCG GTG ACG CCT ACA GTG GCT GTC GCA CAC CCG GGC GCT CCG CTT GAG TCG TTC CGG CGA CAT GTG GAC TTA ATG GTA GGC GCG GCC ACT TTG TGT TCT GCC CTC TAT GTT GGG GAC CTC TGC GGA	39 78 117 156 195 234 273								
20	GGT GCC TTC CTG ATG GGG CAG ATG ATC ACT TTT CGG CCG CGT CGC CAC TGG ACC ACG CAG GAG TGC AAT TGT TCC ATC TAC ACT GGC CAT ATC ACC GGC CAC AGG ATG GCG TGG GAC ATG ATG ATG AAC TGG AGC CCT ACC ACC ACT CTG CTC CTC GCC CAG ATC ATG AGG GTC CCC ACA GCC TTT CTC GAC ATG GTT GCC GGA GGC CAC TGG GGC GTC CTC GCG GGC TTG GCG TAC TTC AGC ATG CAA GGC AAT TGG GCC AAG GTA GTC CTG GTC CTT TTC CTC TTT GCT GGG GTA GAC GCC	312 351 390 429 468 507 546 576								
25	(2) INFORMATION FOR SEQ ID NO:41:									
23	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear									
30	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: homosapiens     (C) INDIVIDUAL ISOLATE: Z1</pre>									
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:									
35	GTG CAC TAC CGG AAT GCT TCG GGC GTC TAT CAT GTC ACC AAT GAT TGC CCT AAC ACC AGC ATA GTG TAC GAG ACG GAG CAC CAC ATC ATG CAC TTG CCA GGG TGT GTC CCC TGT GTG	39 78 117								

35

- 74 -

5	CGG ACG GAG AAT ACT TCT CGC TGC TGG GTG CCC TTG ACC CCC ACT GTG GCC GCG CCC TAT CCC AAC GCA CCG TTA GAG TCC ATG CGC AGG CAT GTA GAC CTG ATG GTG GGT GCG GCT ACT ATG TGT TCC GCC TTC TAC ATT GGA GAT CTG TGT GGA GGC GTC TTC CTA GTG GGC CAG CTG TTC GAC TTC CGA CCG CGC CGG CAC TGG ACC ACC CAG GAT TGC AAC TGC TCC ATC TAT CCT GGT CAC GTC TCG GGC CAC AGG ATG GCC TGG GAC ATG ATG ATG ATG AAC TGG AGC CCT ACC AGC GCG CTG ATT ATG GCT CAG ATC TTA CGG ATC CCC TCT ATC CTA GGT GAC TTG CTC ACC GGG GGT CAC TGG GGA GTT CTT GCT GGT CTA GCT TTC TTC ACC GGG GGT CAC TGG GGA GTT CTT GCT GGT CTA GCT GTC CTG GTC CTA TTC CTA GCT GTC CTG GTC CTA TTC CTA GCT GCT CTA GCT CTG GTC CTA TTC CTA GCT GTC CTA TTC CTA GCT GTC GTC CTA GCT GTC CTA TTC CTA GCT GTC GTC GTC GTC CTA GCT GTC GTC GTC GTC GTC GTC CTA GCT CTA GCT GTC CTA GCT GTC GTC GTC GTC GTC GTC GTC CTA GCT GTC CTA GCT GTC GTC GTC GTC GTC GTC GTC GTC GTC	156 195 234 273 312 351 390 429 468 507 546 576
10	(2) INFORMATION FOR SEQ ID NO:42:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
15	<ul> <li>(vi) ORIGINAL SOURCE:         <ul> <li>(A) ORGANISM: homosapiens</li> <li>(C) INDIVIDUAL ISOLATE: Z6</li> </ul> </li> <li>(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:</li> </ul>	
20	GTT AAC TAT CGC AAT GCC TCG GGC GTC TAT CAC GTC ACC AAC GAC TGC CCG AAC TCG AGC ATA GTG TAT GAG GCC GAA CAC CAG ATC TTA CAC CTC CCA GGG TGC TTG CCC TGT GTG AGG GTT GGG AAT CAG TCA CGC TGC TGG GTG GCC CTT ACT CCC ACC GTG GCG GTG TCT TAT ATC GGT GCT CCG CTT GAC TCC CTC CGG AGA CAT GTG GAC CTG ATG GTG GGC GCC ACT GTA TGC TCT GCC CTC TAC GTT GGA GAT CTG TGC GGT GGT GCA TTC TTG GTT GGC CAG ATG TTC TCC TTC CAG CCG CGA CGC CAC TGG ACT ACG CAG GAC TGC AAT TGT TCT ATC	39 78 117 156 195 234 273 312 351
25	TAC GCA GGG CAT ATC ACG GGC CAC AGG ATG GCA TGG GAC ATG ATG ATG AAC TGG AGT CCC ACA ACC ACC CTG CTT CTC GCC CAG GTC ATG AGG ATC CCT AGC ACT CTG GTA GAT CTA CTC GCT GGA GGG CAC TGG GGC GTC CTT GTT GGG TTG GCG TAC TTC AGT ATG CAA GCT AAT TGG GCC AAA GTC ATC CTG GTC CTT TTC CTC TTC GCT GGA GTT GAT GCC	390 429 468 507 546 576
30	(2) INFORMATION FOR SEQ ID NO:43:	
·	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single	

STRANDEDNESS: single TOPOLOGY: linear

(C) (D)

ORIGINAL SOURCE:

(vi)

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(A)
                          ORGANISM: homosapiens
                          INDIVIDUAL ISOLATE:
                     (C)
           (xi)
                     SEQUENCE DESCRIPTION: SEO ID NO:43:
     GTC AAC TAT CAC AAT GCC TCG GGC GTC TAT CAC ATC ACC
                                                                39
     AAC GAC TGC CCG AAC TCG AGC ATA ATG TAT GAG GCC GAA
                                                                78
     CAC CAC ATC CTA CAC CTC CCA GGG TGC GTA CCC TGT GTG
                                                               117
 5
     AGG GAG GGG AAC CAG TCA CGC TGC TGG GTG GCC CTT ACT
                                                               156
     CCC ACC GTG GCG GCG CCT TAT ATC GGT GCA CCG CTT GAA
                                                               195
     TCC ATC CGG AGA CAT GTG GAC CTG ATG GTA GGC GCT GCT
                                                               234
     ACA GTG TGC TCC GCT CTC TAC ATT GGG GAC CTG TGC GGT
                                                               273
     GGC GTA TIT TTG GTT GGT CAG ATG TTT TCT TTC CAG CCG
                                                               312
     CGA CGC CAC TGG ACT ACG CAG GAC TGC AAT TGT TCC ATC
                                                               351
     TAT GCG GGG CAC GTT ACA GGC CAC AGA ATG GCA TGG GAC
                                                               390
10
     ATG ATG AAC TGG AGT CCC ACA ACC ACC TTG GTC CTC
                                                               429
     GCC CAG GTT ATG AGG ATC CCT AGC ACT CTG GTG GAC CTA
                                                               468
     CTC ACT GGA GGG CAC TGG GGT ATC CTT ATC GGG GTG GCA
                                                               507
     TAC TTC TGC ATG CAA GCT AAT TGG GCC AAG GTC ATT CTG
                                                               546
     GTC CTT TTC CTC TAC GCT GGA GTT GAT GCC
                                                               576
     (2)
          INFORMATION FOR SEQ ID NO:44:
15
                    SEQUENCE CHARACTERISTICS:
           (i)
                     (A)
                         LENGTH: 576 base pairs
                     (B)
                          TYPE: nucleic acid
                     (C)
                          STRANDEDNESS: single
                     (D)
                         TOPOLOGY: linear
20
                    ORIGINAL SOURCE:
          (vi)
                     (A)
                         ORGANISM: homosapiens
                     (C)
                         INDIVIDUAL ISOLATE: DK13
                    SEQUENCE DESCRIPTION: SEO ID NO:44:
          (xi)
     TAC AAC TAT CGC AAC AGC TCG GGT GTC TAC CAT GTC ACC
                                                               39
     AAC GAT TGC CCG AAC TCG AGC ATA GTC TAT GAA ACC GAT
                                                               78
25
     TAC CAC ATC TTA CAC CTC CCG GGA TGC GTT CCT TGC GTG
                                                               117
     AGG GAA GGG AAC AAG TCT ACA TGC TGG GTG TCT CTC ACC
                                                               156
     CCC ACC GTG GCT GCG CAA CAT CTG AAT GCT CCG CTT GAG
     TCT TTG AGA CGT CAC GTG GAT CTG ATG GTG GGC GGC GCC
                                                               234
     ACT CTC TGC TCC GCC CTC TAC ATC GGA GAC GTG TGT GGG
                                                              273
     GGT GTG TTC TTG GTC GGT CAA CTG TTC ACC TTC CAA CCT
                                                              312
     CGC CGC CAC TGG ACC ACC CAA GAC TGC AAT TGT TCC ATC
                                                               351
30
     TAC ACA GGA CAT ATC ACA GGA CAC AGA ATG GCT TGG GAC
                                                               390
     ATG ATG AAT TGG AGC CCC ACT GCG ACG CTG GTC CTC
                                                              429
     GCC CAA CTT ATG AGG ATC CCA GGC GCC ATG GTC GAC CTG
                                                              468
     CTT GCA GGC GGC CAC TGG GGC ATT CTG GTT GGC ATA GCG
                                                              507
     TAC TTC AGC ATG CAA GCT AAT TGG GCC AAG GTT ATC CTG
                                                              546
     GTC CTG TTT CTC TTT GCT GGA GTC GAC GCT
                                                               576
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<sup>35 (2)</sup> INFORMATION FOR SEQ ID NO:45:

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(i)
                    SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH: 576 base pairs
                     (B)
                          TYPE: nucleic acid
                     (C)
                          STRANDEDNESS: single
                     (D)
                          TOPOLOGY: linear
                    ORIGINAL SOURCE:
          (vi)
                     (A)
                          ORGANISM: homosapiens
 5
                     (C)
                          INDIVIDUAL ISOLATE: SA1
                    SEQUENCE DESCRIPTION: SEQ ID NO:45:
          (xi)
     GTT CCC TAC CGG AAT GCC TCT GGG GTT TAC CAT GTC ACC
                                                                39
     AAT GAC TGC CCA AAC TCC TCC ATA GTC TAC GAG GCT GAT
                                                                78
     AGC CTG ATC TTG CAC GCA CCT GGC TGC GTG CCC TGT GTC
                                                               117
10
     AGG CAA GAT AAT GTC AGT AGG TGC TGG GTC CAA ATC ACC
                                                               156
     CCC ACA CTG TCA GCC CCG ACC TTC GGA GCG GTC ACG GCT
                                                                195
     CCT CTT CGG AGG GCC GTT GAC TAC TTA GCG GGA GGA GCT
                                                                234
     GCT CTC TGC TCC GCA CTA TAC GTC GGC GAC GCG TGC GGG
                                                                273
     GCA GTG TTT CTG GTA GGC CAA ATG TTC ACC TAT AGG CCT
                                                                312
     CGC CAG CAT ACC ACA GTG CAG GAC TGC AAC TGT TCC ATT
                                                                351
     TAC AGT GGC CAT ATC ACC GGC CAC CGG ATG GCT TGG GAC
                                                               390
     ATG ATG AAT TGG TCA CCT ACG ACA GCC TTG CTG ATG
                                                               429
15
     GCC CAG ATG CTA CGG ATC CCC CAG GTG GTC ATA GAC ATC
                                                               468
                                                               507
     ATA GCC GGG GGC CAC TGG GGG GTC TTG TTT GCC GCC GCA
     TAC TTT GCG TCG GCC GCC AAC TGG GCT AAG GTA GTG CTG
                                                               546
     GTT CTG TTC CTG TTT GCG GGG GTC GAT GGC
                                                               576
     (2)
          INFORMATION FOR SEQ ID NO:46:
20
                    SEQUENCE CHARACTERISTICS:
          (i)
                          LENGTH: 576 base pairs
                     (A)
                          TYPE: nucleic acid
                     (B)
                     (C)
                          STRANDEDNESS: single
                          TOPOLOGY: linear
                     (D)
                    ORIGINAL SOURCE:
          (vi)
25
                          ORGANISM: homosapiens
                     (A)
                          INDIVIDUAL ISOLATE: SA4
                     (C)
                    SEQUENCE DESCRIPTION: SEQ ID NO:46:
           (xi)
     GTT CCC TAC CGA AAC GCC TCT GGG GTT TAT CAT GTC ACC
                                                                39
     AAT GAT TGC CCA AAC TCT TCC ATA GTT TAC GAG GCT GAT
                                                                78
     AAC CTG ATC TTG CAT GCA CCT GGT TGC GTG CCT TGT GTC
                                                               117
30
     AGG CAA GAT AAT GTC AGT AAG TGC TGG GTC CAA ATC ACC
                                                               156
     CCC ACG TTG TCA GCC CCG AAT CTC GGA GCG GTC ACG GCT
                                                               195
     CCT CTT CGG AGG GCC GTT GAC TAC TTA GCG GGA GGG GCT
                                                               234
     GCC CTC TGC TCC GCA CTA TAC GTC GGG GAC GCG TGC GGG
                                                               273
     GCA GTG TTT TTG GTA GGC CAA ATG TTC ACC TAT AGG CCT
                                                               312
     CGC CAG CAC ACT ACG GTG CAA GAC TGC AAT TGC TCT ATT
                                                               351
     TAC AGT GGC CAT ATC ACC GGC CAC CGG ATG GCA TGG GAC
                                                               390
35
     ATG ATG ATG AAT TGG TCA CCT ACG ACG GCC TTG CTG ATG
```

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0	GCC CAG TTG CTA CGG ATT CCC CAG GTG GTC ATC GAC ATC ATT GCC GGG GGC CAC TGG GGG GTC TTG TTT GCC GCC GCA TAT TTC GCG TCA GCG GCT AAC TGG GCT AAG GTT ATA CTG GTC TTG TTT CTG TTT GCG GGG GTC GAT GCC	468 507 546 576
	(2) INFORMATION FOR SEQ ID NO:47:	
5	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
10	<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: homosapiens</li><li>(C) INDIVIDUAL ISOLATE: SA5</li></ul>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:	
15	GTC CCC TAC CGA AAT GCC TCT GGG GTT TAT CAT GTC ACC AAT GAT TGC CCA AAC TCT TCC ATA GTC TAC GAG GCT GAT AAC CTG ATT CTG CAC GCA CCT GGT TGC GTG CCC TGT GTC AAG GAA GGT AAT GTC AGT AGG TGC TGG GTC CAA ATC ACC CCC ACA TTG TCA GCC CCG AAC CTC GGA GCG GTC ACG GCT CCT CTT CGG AGG GTC GTT GAC TAC TTA GCG GGA GGG GCT GCC CTC TGC TCC GCA CTA TAC GTC GGG GAC GCG TGC GGG GCA GTG TTC TTG GTA GGC CAA ATG TTC ACC TAT AGG CCT	39 78 117 156 195 234 273 312
20	CGC CAG CAT ACT ACG GTG CAG GAC TGC AAC TGT TCC ATT TAC AGC GGC CAT ATC ACC GGC CAC CGA ATG GCA TGG GAC ATG ATG ATG ATG ATG ATG TCA CCT ACG ACA GCC TTG GTG ATG GCC CAG GTG CTA CGG ATT CCC CAA GTG GTC ATT GAC ATC ATT GCC GGG GGC CAC TGG GGG GTC TTG TTC GCC GTC GCA TAC TTC GCG TCA GCG GTC AAC TGG GCT AAC GTG GTC GTG GTC CTG TTT CTG TTT GCG GGG GTC GAT GGC	351 390 429 468 507 546 576
	(2) INFORMATION FOR SEQ ID NO:48:	
25	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 576 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
30	<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: homosapiens</li><li>(C) INDIVIDUAL ISOLATE: SA6</li></ul>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:	
35	GTT CCT TAC CGG AAT GCC TCT GGG GTG TAT CAT GTT ACC AAT GAT TGC CCA AAC TCT TCC ATA GTC TAT GAG GCT GAT GAC CTG ATC CTA CAC GCA CCT GGC TGC GTG CCC TGT GTC CGG AAG GAT AAT GTC AGA TGC TGG GTT CAT ATC ACC	39 78 117 156

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5	CCT CTT CGG AGG GCC GCC CTG TGC TCC GCG GCA TTG TTT TTG GTA CGC CAG CAT GCT ACG TAC AGT GGC CAT ATC ATG ATG ATG AAT TGG GCC CAA ATG CTA CGG ATT GCC GGG GGC CAC	CCG AGC CTC GGA GCG GTC ACG GCT GTT GAT TAC TTG GCG GGA GGG GCC TTA TAC GTC GGA GAC GTG TGC GGG GGC CAA ATG TTC ACC TAT AGG CCT GTA CAG GAC TGC AAC TGC TCC ATT ACT GGC CAC CGG ATG GCA TGG GAC TCA CCC GCG ACA GCC TTG GTG ATG ATT CCC CAG GTG GTC ATT GAC ATC TGG GGG GTC TTG TTC GCC GCT GCA GCT AAC TGG GCT AAG GTT GTG CTG GCG GGG GTT GAT GCC	195 234 273 312 351 390 429 468 507 546 576											
	(2) INFORMATION FOR SEQ ID NO:49:													
10	(A) (B) (C)	ENCE CHARACTERISTICS: LENGTH: 576 base pairs TYPE: nucleic acid STRANDEDNESS: single TOPOLOGY: linear												
15	(A) (C)	INDIVIDUAL ISOLATE: SA7												
	-	NCE DESCRIPTION: SEQ ID NO:49:												
20	AAT GAT TGC CCG AAC AAC CTG ATC CTG CAC AGA CAA AAT AAT GTC CCC ACA TTG TCA GCC CCT CTT CGG AGG GCC GCC CTC TGC TCC GCG GCA GTG TTT TTG GTA	GCC TCC GGG GTT TAT CAT GTC ACC TCT TCC ATA GTC TAT GAG GCT GAC GCA CCT GGT TGC GTG CCC TGT GTC AGT AGG TGC TGG GTC CAA ATC ACC CCG AAC CTC GGA GCG GTC ACG GCT GTT GAC TAC CTA GCG GGA GGG GCT CTA TAC GTC GGG GAC GCG TGC GGG GGC CAG ATG TTC AGC TAT AGG CCT GTG CAG GAC TGC AAC TGT TCC ATT	39 78 117 156 195 234 273 312 351											
25	TAC AGT GGC CAT ATC ATG ATG ATG AAT TGG GCC CAG TTG CTA CGG ATT GCC GGG GGC CAC	ACC GGC CAC CGA ATG GCA TGG GAC TCA CCT ACG ACA GCC TTG GTG ATG ATT CCC CAG GTG GTC ATC GAC ATC TGG GGG GTC TTG TTC GCC GCC GCA GCT AAC TGG GCT AAG GTT GTG CTG	390 429 468 507 546 576											
	(2) INFORMATION FOR	SEQ ID NO:50:												
30	(A) (B) (C)	NCE CHARACTERISTICS: LENGTH: 576 base pairs TYPE: nucleic acid STRANDEDNESS: single TOPOLOGY: linear												
35	(A)	NAL SOURCE: ORGANISM: homosapiens INDIVIDUAL ISOLATE: SA13												

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•	( <b>x</b> i) 5	SEQUENCE	DESCRIPTION: SEQ ID NO:50:	
5	AAT GAT TGC CCA GAC CTG ATC TTA AGG CAG GGT AAT CCC ACA CTG TCA CCT CTT CGG AGG GCC CTT TGC TCC GCA GTG TTT TTG CGC CGG CAT AAT TAC AGT GGC CAC ATG ATG ATG AAT GCC CAG TTG TTA ATT GCC GGG GCC	AAC TCT CAC GCA GTC AGT GCC CCG GCC GTT GCG TTA GTA GGT GTT GTG ATC ACC TGG TCA CGG ATT CAC TGG	AGG TGC TGG GTC CAG ATC ACC AGC CTC GGA GCG GTC ACG GCT GAC TAC TTA GCG GGG GGG GCT TAC GTC GGA GAC GCG TGC GGG CAA ATG TTC ACC TAT AGC CCT CAG GAC TGC AAC TGT TCC ATT GGC CAC CGG ATG GCA TGG GAC CCT ACA ACA GCT TTG GTG ATG CCC CAG GTG GTC ATT GAC ATC GGG GTC TTG TTC GCC GCC GCA	39 78 117 156 195 273 312 351 468 507
	GTC CTG TTT CTG	TIT GCG		576
15	( (	EQUENCE A) LENG B) TYPE C) STRA	CHARACTERISTICS:	
20	()	C) INDI	SOURCE: NISM: homosapiens VIDUAL ISOLATE: HK2 DESCRIPTION: SEQ ID NO:51:	
25	AAT GAT TGC CCC GCT ATG ATC TTG AGG GTC GAT GAT CCC ACC CTG GCC GGA TTC CGC AGG GTG GTT TGC TCA TCT CTC TTT TTG CGC CGT CAT TGG TAT ACA GGC CAC ATG ATG ATG AAC TCT AGC ATC TTG ATA TTT GGT GGC	AAC TCC CAT TTG CAT TTG CAT CCA CAT GTG CAT TGG CAT TG	AGC ATC GTG CTG GAG GCG GAT CCT GGA TGC TTG CCT TGT GTG ACC TGT TGG CAT GCT GTG ACC AAT GCT TCC ACG CCC GCA ACG AAT CTT CTT GCG GGC GCC GCA ACC ATC GGG GAC CTG TGT GGC CAA CTA TTC ACC TTT CAG CCC CAA GAC TGC AAC TGC TCC ATC GGC CAC AGG ATG GCT TGG GAC CCC ACA ACC ACT CTG GTC CTA CCT GAG ATT TGT GCG AGT GTG GGG ATA CTA CTA GCC GTT GCC 5 GGG ATA CTA CTA GCC GTT GCC 5 GGG ATA CTA CTA GCC GTT GCC	39 78 17 56 95 34 73 12 50 68 07
	TAC TTT GGC ATG CGTT CTG TTC CTA	GCT GGC 1	AAC TGG CTA AAA GTT CTG GCT 54	46 76
٠	(2) INFORMATION	FOR SEQ	ID NO:52:	

35 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 192 amino acids

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- - - O
                        (B)
                             TYPE: amino acid
                        (C)
                             STRANDEDNESS: unknown
                             TOPOLOGY: unknown
                        (D)
              (vi)
                        ORIGINAL SOURCE:
                             ORGANISM:
                        (A)
                                        homosapiens
                        (C)
                             INDIVIDUAL ISOLATE:
    5
              (xi)
                        SEQUENCE DESCRIPTION: SEQ ID NO:52:
        Tyr Gln Val Arg Asn Ser Thr Gly Leu Tyr His Val Thr Asn Asp
                                                                   15
        Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Ala Ile Leu
        His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Gly Asn Val Ser
   10
                          35
        Arg Cys Trp Val Ala Met Thr Pro Thr Val Ala Thr Arg Asp Gly
                                              55
        Lys Leu Pro Thr Ala Gln Leu Arg Arg His Ile Asp Leu Leu Val
                          65
                                              70
        Gly Ser Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys
                          80
                                              85
        Gly Ser Val Phe Leu Val Gly Gln Leu Phe Thr Phe Ser Pro Arq
   15
                          95
                                             100
                                                                  105
        Arg His Trp Thr Thr Gln Gly Cys Asn Cys Ser Ile Tyr Pro Gly
                         110
                                             115
                                                                  120
        His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                         125
                                             130
                                                                  135
        Ser Pro Thr Thr Ala Leu Val Val Ala Gln Leu Leu Arg Ile Pro
                         140
                                             145
   20
        Gln Ala Ile Leu Asp Met Ile Ala Gly Ala His Trp Gly Val Leu
                         155
                                             160
        Ala Gly Ile Ala Tyr Phe Ser Met Val Gly Asn Trp Ala Lys Val
                                             175
                                                                  180
        Leu Val Val Leu Leu Phe Ala Gly Val Asp Ala
                         185
  25
        (2)
             INFORMATION FOR SEQ ID NO:53:
             (i)
                        SEQUENCE CHARACTERISTICS:
                        (A)
                             LENGTH: 192 amino acids
                        (B)
                             TYPE: amino acid
                        (C)
                             STRANDEDNESS: unknown
                             TOPOLOGY:
                        (D)
                                       unknown
  30
             (vi)
                        ORIGINAL SOURCE:
                        (A)
                             ORGANISM: homosapiens
                             INDIVIDUAL ISOLATE: DK9
                        (C)
             (xi)
                       SEQUENCE DESCRIPTION: SEQ ID NO:53:
        Tyr Gln Val Arg Asn Ser Ser Gly Leu Tyr His Val Thr Asn Asp
  35
```

105

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Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Ala Ile Leu
      His Ser Pro Gly Cys Val Pro Cys Val Arg Glu Gly Asn Ala Ser
                                            40
      Lys Cys Trp Val Ala Val Ala Pro Thr Val Ala Thr Arg Asp Gly
                                           55
      Lys Leu Pro Ala Thr Gln Leu Arg Arg His Ile Asp Leu Leu Val
                       65
                                            70
 5
     Gly Ser Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys
                                            85
                                                                90
     Gly Ser Val Phe Leu Val Gly Gln Leu Phe Thr Phe Ser Pro Arg
                                                               105
     Arg His Trp Thr Thr Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                                           115
                                                               120
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
10
                      125
                                           130
     Ser Pro Thr Ala Ala Leu Val Met Ala Gln Leu Leu Arg Ile Pro
                      140
                                           145
                                                               150
     Gln Ala Ile Leu Asp Met Ile Ala Gly Ala His Trp Gly Val Leu
                      155
                                           160
     Ala Gly Ile Ala Tyr Phe Ser Met Val Gly Asn Trp Ala Lys Val
                      170
                                          175
     Val Val Leu Leu Leu Phe Thr Gly Val Asp Ala
15
                      185
      (2)
           INFORMATION FOR SEQ ID NO:54:
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH:
                                  192 amino acids
20
                     (B)
                          TYPE:
                                 amino acid
                     (C)
                          STRANDEDNESS:
                     (D)
                          TOPOLOGY:
                                     unknown
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE:
                                              DR1
25
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:54:
     His Gln Val Arg Asn Ser Thr Gly Leu Tyr His Val Thr Asn Asp
     Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Ala Ile Leu
                       20
                                           25
     His Ala Pro Gly Cys Val Pro Cys Val Arg Glu Gly Asn Ala Ser
30
                                                                45
     Arg Cys Trp Val Ala Val Thr Pro Thr Val Ala Thr Arg Asp Gly
                                           55
                                                                60
     Lys Leu Pro Thr Thr Gln Leu Arg Arg His Ile Asp Leu Leu Val
                                           70
     Gly Ser Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys
                       80
                                           85
     Gly Ser Val Phe Leu Val Gly Gln Leu Phe Thr Phe Ser Pro Arg
35
```

95

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Arg His Trp Thr Thr Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                                          115
                                                               120
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                                          130
                                                               135
     Ser Pro Thr Thr Ala Leu Val Met Ala Gln Leu Leu Arg Ile Pro
                                          145
                                                               150
     Gln Ala Ile Leu Asp Met Ile Ala Gly Ala His Trp Gly Val Leu
                      155
                                                               165
                                          160
 5
     Ala Gly Ile Ala Tyr Phe Ser Met Val Gly Asn Trp Ala Lys Val
                      170
                                          175
     Val Val Leu Leu Leu Phe Ala Gly Val Asp Ala
     (2)
          INFORMATION FOR SEQ ID NO:55:
10
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH:
                                  192 amino acids
                     (B)
                          TYPE:
                                 amino acid
                     (C)
                          STRANDEDNESS: unknown
                     (D)
                          TOPOLOGY: unknown
           (vi)
                     ORIGINAL SOURCE:
15
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE:
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:55:
     His Gln Val Arg Asn Ser Thr Gly Leu Tyr His Val Thr Asn Asp
20
     Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Ala Ile Leu
     His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Gly Asn Thr Ser
                                                                45
     Arg Cys Trp Val Ala Val Thr Pro Thr Val Ala Thr Arg Asp Gly
                       50
                                           55
     Lys Leu Pro Thr Thr Gln Leu Arg Arg His Ile Asp Leu Leu Val
                                           70
                                                                75
25
     Gly Ser Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys
                                                                90
                       80
     Gly Ser Val Phe Leu Val Gly Gln Leu Phe Thr Phe Ser Pro Arg
                                          100
                       95
                                                               105
     His His Trp Thr Thr Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                          115
                                                               120
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
30
                      125
                                          130
                                                               135
     Ser Pro Thr Thr Ala Leu Val Val Ala Gln Leu Leu Arg Ile Pro
                      140
                                          145
                                                              150
     Gln Ala Ile Leu Asp Met Ile Ala Gly Ala His Trp Gly Val Leu
                      155
                                          160
     Ala Gly Ile Ala Tyr Phe Ser Met Val Gly Asn Trp Ala Lys Val
                      170
                                          175
     Leu Val Val Leu Leu Phe Ala Gly Val Asp Ala
35
```

190

185

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```
(2)
           INFORMATION FOR SEQ ID NO:56:
           (i)
                     SEQUENCE CHARACTERISTICS:
                          LENGTH:
                                   192 amino acids
                      (B)
                          TYPE: amino acid
                          STRANDEDNESS: unknown
                      (C)
                      (D)
                          TOPOLOGY: unknown
 5
           (vi)
                     ORIGINAL SOURCE:
                      (A)
                          ORGANISM:
                                    homosapiens
                     (C)
                          INDIVIDUAL ISOLATE:
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:56:
10
      Tyr Gln Val Arg Asn Ser Thr Gly Leu Tyr His Val Thr Asn Asp
                                            10
     Cys Pro Asn Ser Ser Ile Val Tyr Glu Thr Ala Asp Ala Ile Leu
                       20
                                            25
     His Ala Pro Gly Cys Val Pro Cys Val Arg Glu Gly Asn Thr Ser
                       35
                                            40
     Arg Cys Trp Val Ala Met Thr Pro Thr Val Ala Thr Arg Asp Gly
                       50
                                            55
15
     Lys Leu Pro Ala Thr Gln Leu Arg Arg Tyr Ile Asp Leu Leu Val
                                            70
                       65
                                                                75
     Gly Ser Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys
                       80
                                            85
                                                                90
     Gly Ser Val Phe Leu Val Gly Gln Leu Phe Thr Phe Ser Pro Arq
                                           100
                                                               105
     Arg Leu Trp Thr Thr Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
20
                      110
                                           115
                                                               120
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                                           130
                                                               135
     Ser Pro Thr Thr Ala Leu Val Val Ala Gln Leu Leu Arg Ile Pro
                                                               150
     Gln Ala Ile Leu Asp Met Ile Ala Gly Ala His Trp Gly Val Leu
                                           160
     Ala Gly Ile Ala Tyr Phe Ser Met Val Gly Asn Trp Ala Lys Val
25
                      170
                                          175
     Leu Val Val Leu Leu Phe Ala Gly Val Asp Ala
                      185
      (2)
          INFORMATION FOR SEQ ID NO:57:
30
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH: 192 amino acids
                     (B)
                          TYPE: amino acid
                     (C)
                          STRANDEDNESS: unknown
                     (D)
                          TOPOLOGY: unknown
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
35
                     (C)
                          INDIVIDUAL ISOLATE:
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0
           (xi)
                     SEQUENCE DESCRIPTION: SEO ID NO:57:
      Tyr Gln Val Arg Asn Ser Thr Gly Leu Tyr His Val Thr Asn Asp
      Cys Pro Asn Ser Ser Ile Val Tyr Glu Thr Ala Asp Thr Ile Leu
     His Ser Pro Gly Cys Val Pro Cys Val Arg Glu Gly Asn Ala Ser
                                                                45
 5
     Arg Cys Trp Val Pro Val Ala Pro Thr Val Ala Thr Arg Asp Gly
     Lys Leu Pro Ala Thr Gln Leu Arg Arg His Ile Asp Leu Leu Val
     Gly Ser Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys
                                           85
                                                                90
     Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Ile Ser Pro Arg
10
                                          100
                                                               105
     Arg His Trp Thr Thr Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                          115
                                                               120
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                      125
                                          130
                                                               135
     Ser Pro Thr Thr Ala Leu Val Ile Ala Gln Leu Leu Arg Val Pro
                      140
                                          145
                                                               150
     Gln Ala Val Leu Asp Met Ile Ala Gly Ala His Trp Gly Val Leu
15
                      155
                                          160
     Ala Gly Ile Ala Tyr Phe Ser Met Ala Gly Asn Trp Ala Lys Val
                      170
                                          175
     Leu Leu Val Leu Leu Phe Ala Gly Val Asp Ala
                      185
20
     (2)
          INFORMATION FOR SEO ID NO:58:
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH:
                                  192 amino acids
                     (B)
                          TYPE: amino acid
                     (C)
                          STRANDEDNESS: unknown
                     (D)
                          TOPOLOGY: unknown
25
           (vi)
                    ORIGINAL SOURCE:
                          ORGANISM: homosapiens
                     (A)
                     (C)
                          INDIVIDUAL ISOLATE:
          (xi)
                    SEQUENCE DESCRIPTION: SEQ ID NO:58:
     Tyr Gln Val Arg Asn Ser Ser Gly Leu Tyr His Val Thr Asn Asp
30
                                           10
     Cys Pro Asn Ser Ser Ile Val Tyr Glu Thr Ala Asp Ala Ile Leu
                      20
                                           25
     His Ser Pro Gly Cys Val Pro Cys Val Arg Glu Asp Gly Ala Pro
                       35
     Lys Cys Trp Val Ala Val Ala Pro Thr Val Ala Thr Arg Asp Gly
                                           55
     Lys Leu Pro Ala Thr Gln Leu Arg Arg His Ile Asp Leu Leu Val
35
                      65
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0	Gly	Ser	Ala	Thr	Leu 80	Cys	Ser	Ala	Leu	Tyr 85	Val	Gly	Asp	Leu	Cys
	Gly	Ser	Val	Phe	Leu 95	Val	Ser	Gln	Leu	Phe 100	Thr	Phe	Ser	Pro	Arg
•	Arg	His	Trp	Thr	Thr 110	Gln	Asp	Cys	Asn	Cys 115	Ser	Ile	Tyr	Pro	Gly 120
5	His	Ile	Thr	Gly	His 125	Arg	Met	Ala	Trp	Asp 130	Met	Met	Met	Asn	Trp 135
3	Ser	Pro	Thr	Thr	Ala 140	Leu	Val	Val	Ala	Gln 145	Leu	Leu	Arg	Ile	Pro
	Gln	Ala	Val	Leu	<b>Asp</b> 155	Met	Ile	Ala	Gly	Ala 160	His	Trp	Gly	Val	Leu 165
	Ala	Gly	Ile	Ala	Tyr 170	Phe	Ser	Met	Val	Gly 175	Asn	Trp	Ala	Lys	Val 180
10	Leu	Ile	Val	Leu	Leu 185	Leu	Phe	Ser	Gly	Val 190	Asp	Ala			

# (2) INFORMATION FOR SEQ ID NO:59:

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 192 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: unknown

(D) TOPOLOGY: unknown

(vi) ORIGINAL SOURCE:

(A) ORGANISM: homosapiens

(C) INDIVIDUAL ISOLATE: US11

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

```
Tyr Gln Val Arg Asn Ser Thr Gly Leu Tyr His Val Thr Asn Asp
                                                                15
     Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Ala Ile Leu
                                                                30
     His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Gly Asn Ala Ser
                                                                45
25
     Arg Cys Trp Val Ala Met Thr Pro Thr Val Ala Thr Arg Asp Gly
                       50
                                           55
                                                                60
     Lys Leu Pro Thr Thr Gln Leu Arg Arg His Ile Asp Leu Leu Val
                       65
                                           70
     Gly Ser Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys
                       80
                                           85
                                                                90
     Gly Ser Val Phe Leu Val Gly Gln Leu Phe Thr Phe Ser Pro Arg
30
                       95
                                          100
                                                               105
     Arg His Trp Thr Thr Gln Gly Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                          115
                                                               120
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                      125
                                          130
                                                               135
     Ser Pro Thr Ala Ala Leu Val Val Ala Gln Leu Leu Arg Ile Pro
                                          145
                                                               150
                      140
     Gln Ala Ile Leu Asp Met Ile Ala Gly Ala His Trp Gly Val Leu
35
```

10

35

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Ala Gly Ile Ala Tyr Phe Ser Met Val Gly Asn Trp Ala Lys Val 170 175 180

Leu Val Val Leu Leu Phe Ala Gly Val Asp Ala 185 190

(2) INFORMATION FOR SEQ ID NO:60:

5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 192 amino acids
(B) TYPE: amino acid

(C) STRANDEDNESS: unknown

(D) TOPOLOGY: unknown

(vi) ORIGINAL SOURCE:

(A) ORGANISM: homosapiens

(C) INDIVIDUAL ISOLATE: D1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

Tyr Glu Val Arg Asn Val Ser Gly Val Tyr His Val Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Thr Ala Asp Met Ile Met 15 20 25 His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Asp Asn Ser Ser 35 40 Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Gly 50 55 Asn Val Pro Thr Thr Ala Ile Arg Arg His Val Asp Leu Leu Val 65 70 Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys 20 85 90 Gly Ser Val Phe Leu Ile Ser Gln Leu Phe Thr Leu Ser Pro Arg 105 100 Arg His Glu Thr Val Gln Glu Cys Asn Cys Ser Ile Tyr Pro Gly 115 120 His Val Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp 130 135 25 Ser Pro Thr Thr Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro 150 140 145 Gln Ala Val Met Asp Met Val Ala Gly Ala His Trp Gly Val Leu 155 160 Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val 170 175 180 Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly 30 185 190

## (2) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 192 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: unknown

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```
٥
                      (D)
                           TOPOLOGY: unknown
           (vi)
                     ORIGINAL SOURCE:
                      (A)
                           ORGANISM: homosapiens
                      (C)
                          INDIVIDUAL ISOLATE: D3
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:61:
 5
      Tyr Glu Val Arg Asn Val Ser Gly Val Tyr Gln Val Thr Asn Asp
      Cys Ser Asn Ser Ser Ile Val Tyr Glu Thr Ala Asp Met Ile Met
      His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Asp Asn Ser Ser
                       35
                                            40
      Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Ser
.10
                       50
      Ser Val Pro Thr Thr Thr Ile Arg Arg His Val Asp Leu Leu Val
                       65
                                            70
      Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys
                       80
                                            85
                                                                 90
     Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arg
                       95
                                           100
                                                                105
     Arg His Glu Thr Val Gln Glu Cys Asn Cys Ser Ile Tyr Pro Gly
15
                      110
                                           115
                                                               120
     His Val Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                                           130
                                                                135
      Ser Pro Thr Ala Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro
                      140
     Gln Ala Val Val Asp Met Val Ala Gly Ala His Trp Gly Val Leu
                      155
     Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val
20
                      170
                                           175
                                                               180
     Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly
                      185
      (2)
          INFORMATION FOR SEQ ID NO:62:
25
           (i)
                     SEQUENCE CHARACTERISTICS:
                          LENGTH: 192 amino acids
                     (A)
                     (B)
                          TYPE: amino acid
                     (C)
                          STRANDEDNESS: unknown
                     (D)
                          TOPOLOGY:
                                    unknown
                     ORIGINAL SOURCE:
           (vi)
30
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE: DK1
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:62:
     Tyr Glu Val Arg Asn Val Ser Gly Val Tyr His Val Thr Asn Asp
                                           10
     Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Val Asp Val Ile Met
35
```

```
His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Asn Asn His Ser
     Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Ala
                       50
     Ser Ile Pro Thr Thr Thr Ile Arg Arg His Val Asp Leu Leu Val
     Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys
                                                                90
 5
     Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arg
                                                               105
                                          100
     Arg His Glu Thr Ala Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                          115
                                                               120
     His Val Ser Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                      125
                                          130
     Ser Pro Thr Thr Ala Leu Val Leu Ser Gln Leu Leu Arg Ile Pro
10
                      140
                                          145
     Gln Ala Val Val Asp Met Val Ala Gly Ala His Trp Gly Val Leu
                      155
                                          160
                                                               165
     Ala Gly Leu Ala Tyr Tyr Ser Met Ala Gly Asn Trp Ala Lys Val
                      170
                                          175
     Leu Ile Val Leu Leu Phe Ala Gly Val Asp Gly
                      185
15
      (2)
           INFORMATION FOR SEQ ID NO:63:
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH: 192 amino acids
                     (B)
                          TYPE: amino acid
                     (C)
                          STRANDEDNESS: unknown
20
                     (D)
                          TOPOLOGY: unknown
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE: HK3
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:63:
25
     Tyr Glu Val Arg Asn Val Ser Gly Ile Tyr His Val Thr Asn Asp
     Cys Ser Asn Ser Ser Val Val Tyr Glu Thr Ala Asp Met Ile Met
     His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Asn Asn Ser Ser
     Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Val
30
                                           55
     Ser Val Pro Thr Thr Ile Arg Arg His Val Asp Leu Leu Val
                       65
                                           70
                                                                75
     Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys
                       80
     Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arg
                                          100
                       95
                                                               105
     Arg His Glu Thr Val Gln Asp Cys Asn Cys Ser Leu Tyr Pro Gly
35
                      110
```

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His Val Ser Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp 125 130 Ser Pro Thr Ala Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro 140 145 Gln Ala Val Val Asp Met Val Ala Gly Ala His Trp Gly Val Leu 155 160 165 Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val 170 175 5 Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly 185

## (2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 192 amino acids

(B) TYPE: amino acid

- (C) STRANDEDNESS: unknown
- (D) TOPOLOGY: unknown
- (vi) ORIGINAL SOURCE:

185

- (A) ORGANISM: homosapiens
- (C) INDIVIDUAL ISOLATE: HK4
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

His Glu Val His Asn Val Ser Gly Ile Tyr His Val Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Met Ile Met 20 His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Asn Asn Ser Ser Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Ala Ser Ile Pro Thr Thr Thr Ile Arg Arg His Val Asp Leu Leu Val 75 Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys 85 90 25 Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arg 95 100 105 Arg His Glu Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly 110 115 120 His Val Ser Gly His Arg Met Ala Trp Asp Met Met Asn Trp 125 130 Ser Pro Thr Ala Ala Leu Val Val Ser Gln Leu Leu Arg Leu Pro 30 140 145 150 Gln Ala Val Met Asp Met Val Ala Gly Ala His Trp Gly Val Leu 155 160 Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val 170 175 180 Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly

10

15

INFORMATION FOR SEQ ID NO:65:

(2)

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```
(i)
                     SEQUENCE CHARACTERISTICS:
                          LENGTH: 192 amino acids
                     (B)
                          TYPE:
                                 amino acid
                          STRANDEDNESS: unknown
                     (C)
                          TOPOLOGY: unknown
                     (D)
 5
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE: HK5
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:65:
     Tyr Glu Val Arg Asn Val Ser Gly Val Tyr His Val Thr Asn Asp
10
                                           10
     Cys Ser Asn Leu Ser Ile Val Tyr Glu Thr Thr Asp Met Ile Met
                                           25
     His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Asn Asn Ser Ser
                       35
                                           40
     Arg Cys Trp Val Ala Leu Ala Pro Thr Leu Ala Ala Arg Asn Ala
     Ser Val Pro Thr Thr Ala Ile Arg Arg His Val Asp Leu Leu Val
15
                       65
                                           70
     Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys
                       80
                                           85
     Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arg
                       95
                                          100
     Arg His Glu Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                          115
     His Val Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
20
                                          130
     Ser Pro Thr Thr Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro
                      140
     Gln Ala Val Val Asp Met Val Ala Gly Ala His Trp Gly Val Leu
     Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val
                      170
25
     Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly
                      185
          INFORMATION FOR SEQ ID NO:66:
     (2)
          (i)
                     SEQUENCE CHARACTERISTICS:
30
                         LENGTH: 192 amino acids
                     (A)
                     (B)
                          TYPE: amino acid
                     (C)
                          STRANDEDNESS: unknown
                     (D)
                         TOPOLOGY: unknown
          (vi)
                    ORIGINAL SOURCE:
                     (A)
                         ORGANISM: homosapiens
                     (C)
                         INDIVIDUAL ISOLATE: HK8
35
```

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```
SEQUENCE DESCRIPTION: SEQ ID NO:66:
           (xi)
     Tyr Glu Val Arg Asn Val Ser Gly Ile Tyr His Val Thr Asn Asp
     Cys Ser Asn Ser Ser Ile Val Tyr Glu Thr Ala Asp Met Ile Met
     His Thr Pro Gly Cys Met Pro Cys Val Arg Glu Asn Asn Ser Ser
 5
                                                                45
     Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Val
     Ser Val Pro Thr Thr Ile Arg Arg His Val Asp Leu Leu Val
     Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys
                       80
                                            85
     Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arg
10
                       95
                                          100
                                                               105
     Arg His Glu Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                          115
                                                               120
     His Val Ser Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                      125
                                          130
                                                               135
     Ser Pro Thr Thr Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro
                      140
                                          145
     Gln Ala Ile Val Asp Met Val Ala Gly Ala His Trp Gly Val Leu
15
                      155
                                          160
     Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val
                      170
                                          175
     Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly
                      185
20
     (2)
          INFORMATION FOR SEQ ID NO:67:
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH:
                                  192 amino acids
                     (B)
                          TYPE:
                                 amino acid
                     (C)
                          STRANDEDNESS:
                                         unknown
                          TOPOLOGY:
                     (D)
                                     unknown
25
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE:
           (xi)
                     SEQUENCE DESCRIPTION: SEO ID NO:67:
     Tyr Glu Val Arg Asn Val Ser Gly Val Tyr His Val Thr Asn Asp
30
     Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Met Ile Met
                       20
     His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Gly Asn Ser Ser
                                           40
     Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Ala
                       50
                                           55
     Ser Val Ser Thr Thr Thr Ile Arg His His Val Asp Leu Leu Val
35
                       65
                                           70
```

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15

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0	Gly	Ala	Ala	Ala	Phe 80	Cys	Ser	Ala	Met	Tyr 85	Val	Gly	Asp	Leu	Cys 90
	Gly	Ser	Val	Phe	Leu 95	Val	Ser	Gln	Leu	Phe 100	Thr	Phe	Ser	Pro	Arg
	Arg	His	Glu	Thr	Val 110	Gln	Asp	Cys	Asn	Cys 115	Ser	Ile	Tyr	Pro	Gly 120
5	His	Val	Ser	Gly	His 125	Arg	Met	Ala	Trp	Asp 130	Met	Met	Met	Asn	Trp 135
3	Ser	Pro	Thr	Ala	Ala 140	Leu	Val	Val	Ser	Gln 145	Leu	Leu	Arg	Ile	Pro 150
	Gln	Ala	Val	Val	<b>Asp</b> 155	Met	Val	Ala	Gly	Ala 160	His	Trp	Gly	Ile	Leu 165
	Ala	Gly	Leu	Ala	Tyr 170	Tyr	Ser	Met	Val	Gly 175	Asn	Trp	Ala	Lys	Val 180
10	Leu	Ile	Val	Met	Leu 185	Leu	Phe	Ala	Gly	Val 190	Asp	Gly			

#### (2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 192 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: unknown

(D) TOPOLOGY: unknown

(vi) ORIGINAL SOURCE:

(A) ORGANISM: homosapiens

(C) INDIVIDUAL ISOLATE: IND8

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

Tyr Glu Val Arg Asn Val Ser Gly Val Tyr His Val Thr Asn Asp 10 Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Met Ile Met 20 25 His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Gly Asn Phe Ser 25 Ser Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Ala Ser Val Pro Thr Thr Ile Arg Arg His Val Asp Leu Leu Val Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys 90 Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arg 30 105 95 100 Arg His Glu Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly 110 120 115 His Val Ser Gly His Arg Met Ala Trp Asp Met Met Asn Trp 125 130 Ser Pro Thr Ala Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro 140 145 150 Gln Ala Val Val Asp Met Val Ala Gly Ala His Trp Gly Ile Leu 35 155 160

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Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val
170 175 180
Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly
185 190

### (2) INFORMATION FOR SEO ID NO:69:

5

10

(i)

- SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 192 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: unknown
  - (D) TOPOLOGY: unknown
- (vi) ORIGINAL SOURCE:

(A) ORGANISM: homosapiens

- (C) INDIVIDUAL ISOLATE: P10
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

Tyr Glu Val Arg Asn Val Ser Gly Val Tyr His Val Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Met Ile Met 15 25 His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Asn Asn Ser Ser 35 40 Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Ser 50 Ser Val Pro Thr Thr Ala Ile Arg Arg His Val Asp Leu Leu Val 65 Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys 20 80 90 Gly Ser Val Leu Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arg 105 Arg His Trp Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly 115 120 His Val Ser Gly His Arg Met Ala Trp Asp Met Met Asn Trp 130 135 25 Ser Pro Thr Ala Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro 140 145 Gln Ala Ile Leu Asp Val Val Ala Gly Ala His Trp Gly Val Leu 155 160 Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val 170 175 180 Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly 30 185 190

## (2) INFORMATION FOR SEQ ID NO:70:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 192 amino acids
- (B) TYPE: amino acid
- 35 (C) STRANDEDNESS: unknown

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```
(D) TOPOLOGY: unknown
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE:
                     SEQUENCE DESCRIPTION: SEQ ID NO:70:
           (xi)
 5
     Tyr Glu Val Arg Asn Val Ser Gly Ala Tyr His Val Thr Asn Asp
                                            10
     Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Val Ile Met
     His Thr Pro Gly Cys Val Pro Cys Val Glu Glu Gly Asn Ser Ser
     Gln Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Ala
10
                                            55
     Thr Val Pro Thr Thr Ile Arg Arg His Val Asp Leu Leu Val
                                                                75
                       65
                                           70
     Gly Ala Ala Val Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys
                       80
                                            85
                                                                90
     Gly Ser Val Phe Leu Ile Ser Gln Leu Phe Thr Ile Ser Pro Arg
                                                               105
                       95
                                          100
     Arg His Glu Thr Val Gln Asn Cys Asn Cys Ser Ile Tyr Pro Gly
15
                      110
                                          115
                                                               120
     His Val Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                                          130
                                                               135
                      125
     Ser Pro Thr Thr Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro
                      140
                                          145
                                                               150
     Gln Ala Val Met Asp Met Val Ala Gly Ala His Trp Gly Val Leu
                      155
                                          160
     Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val
20
                      170
                                          175
                                                               180
     Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly
                      185
     (2)
          INFORMATION FOR SEO ID NO:71:
25
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH:
                                   192 amino acids
                     (B)
                          TYPE: amino acid
                     (C)
                          STRANDEDNESS: unknown
                          TOPOLOGY: unknown
           (vi)
                     ORIGINAL SOURCE:
30
                     (A)
                          ORGANISM: homosapiens
                          INDIVIDUAL ISOLATE: $45
                     (C)
                     SEQUENCE DESCRIPTION: SEQ ID NO:71:
           (xi)
     Tyr Glu Val Arg Asn Val Ser Gly Ala Tyr His Val Thr Asn Asp
                                           10
     Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Val Asp Val Ile Leu
35
                                                                30
                       20
                                           25
```

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```
His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Asn Asn Ser Ser
                        35
                                            40
     Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Ser
                       50
                                            55
      Ser Val Pro Thr Thr Thr Ile Arg Arg His Val Asp Leu Leu Val
     Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys
                                                                 90
 5
     Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arq
                                           100
                                                                105
     Arg His Glu Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                           115
                                                                120
     His Val Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                      125
                                           130
                                                                135
     Ser Pro Thr Ala Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro
10
                      140
                                           145
                                                                150
     Gln Ala Val Val Asp Met Val Ala Gly Ala His Trp Gly Val Leu
                      155
                                           160
     Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val
                      170
                                           175
     Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly
15
           INFORMATION FOR SEQ ID NO:72:
      (2)
           (i)
                     SEQUENCE CHARACTERISTICS:
                          LENGTH:
                                   192 amino acids
                     (B)
                          TYPE:
                                 amino acid
                     (C)
                          STRANDEDNESS: unknown
                     (D)
                          TOPOLOGY:
                                     unknown
20
           (vi)
                     ORIGINAL SOURCE:
                          ORGANISM:
                     (A)
                                     homosapiens
                     (C)
                          INDIVIDUAL ISOLATE:
           (xi)
                     SEQUENCE DESCRIPTION: SEO ID NO:72:
     Tyr Glu Val Arg Asn Val Ser Gly Met Tyr His Val Thr Asn Asp
25
                                                                15
     Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Met Ile Met
                                            25
     His Thr Pro Gly Cys Val Pro Cys Val Arq Glu Asn Asn Ser Ser
                                            40
     Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Ser
                       50
                                            55
30
     Ser Val Pro Thr Thr Ile Arg Arg His Val Asp Leu Leu Val
                                                                75
                       65
                                            70
     Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys
                       80
                                            85
                                                                90
     Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arg
                                           100
     Arg Tyr Glu Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                           115
35
```

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Arg Val Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp 125 130 Ser Pro Thr Thr Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro 140 145 Gln Ala Ile Val Asp Met Val Ala Gly Ala His Trp Gly Val Leu 155 160 Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val 170 175 180 5 Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly 185 190

# (2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 192 amino acids

(A) LENGTH: 192 amino acids(B) TYPE: amino acid

- (C) STRANDEDNESS: unknown
- (D) TOPOLOGY: unknown
- (vi) ORIGINAL SOURCE:

185

1

- (A) ORGANISM: homosapiens
- (C) INDIVIDUAL ISOLATE: SW2
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

Tyr Glu Val Arg Asn Val Ser Gly Val Tyr His Val Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Thr Ala Asp Met Ile Met 20 25 His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Ala Asn Ser Ser 20 35 40 Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Thr 50 55 Ser Val Pro Thr Thr Thr Ile Arg Arg His Val Asp Leu Leu Val 65 70 Gly Ala Ala Ala Phe Cys Ser Val Met Tyr Val Gly Asp Leu Cys 85 25 Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arg Arq His Glu Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly 120 His Val Ser Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp 130 135 Ser Pro Thr Ala Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro 30 140 145 150 Gln Ala Val Val Asp Met Val Ala Gly Ala His Trp Gly Val Leu 155 160 Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val 170 175 180 Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly

190

35

15

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```
(2)
           INFORMATION FOR SEQ ID NO:74:
           (i)
                     SEQUENCE CHARACTERISTICS:
                      (A)
                          LENGTH:
                                   192 amino acids
                      (B)
                                 amino acid
                           TYPE:
                           STRANDEDNESS: unknown
                      (C)
                          TOPOLOGY:
                      (D)
                                     unknown
 5
           (vi)
                     ORIGINAL SOURCE:
                          ORGANISM:
                                      homosapiens
                      (C)
                           INDIVIDUAL ISOLATE:
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:74:
     Tyr Glu Val Arg Asn Val Ser Gly Val Tyr Tyr Val Thr Asn Asp
10
                                            10
                                                                 15
     Cys Ser Asn Ser Ser Ile Val Tyr Glu Thr Ala Asp Met Ile Met
                                            25
     His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Ser Asn Ser Ser
                                            40
     Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Ala
                       50
                                            55
     Ser Val Pro Thr Lys Thr Ile Arg Arg His Val Asp Leu Leu Val
15
                       65
                                            70
     Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys
                       80
                                            85
                                                                 90
     Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arg
                       95
                                           100
                                                                105
     Arg His Glu Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                           115
                                                                120
20
     His Val Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                      125
                                           130
                                                                135
     Ser Pro Thr Thr Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro
                      140
                                           145
     Gln Ala Val Val Asp Met Val Ala Gly Ala His Trp Gly Val Leu
                      155
                                           160
     Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val
                                           175
                      170
                                                                180
25
     Leu Ile Val Leu Leu Phe Ala Gly Val Asp Gly
                      185
                                           190
     (2)
          INFORMATION FOR SEQ ID NO:75:
           (i)
                     SEQUENCE CHARACTERISTICS:
                          LENGTH: 192 amino acids
30
                     (A)
                     (B)
                          TYPE: amino acid
                     (C)
                          STRANDEDNESS: unknown
                     (D)
                          TOPOLOGY:
                                     unknown
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                          INDIVIDUAL ISOLATE: T10
                     (C)
35
```

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```
(xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:75:
     Tyr Glu Val Arg Asn Val Ser Gly Met Tyr His Val Thr Asn Asp
                                                                15
     Cys Ser Asn Ser Ser Ile Val Phe Glu Ala Ala Asp Leu Ile Met
     His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Gly Asn Ser Ser
     Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Thr
                       50
                                           55
     Ser Val Pro Thr Thr Ile Arg Arg His Val Asp Leu Leu Val
                       65
     Gly Ala Ala Ala Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys
                       80
                                           85
     Gly Ser Val Phe Leu Val Ser Gln Leu Phe Thr Phe Ser Pro Arg
10
                       95
                                          100
     Arg His Glu Thr Leu Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                                          115
     His Leu Ser Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                                                               135
                                          130
     Ser Pro Thr Thr Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro
                      140
     Gln Ala Val Met Asp Met Val Thr Gly Ala His Trp Gly Val Leu
15
     Ala Gly Leu Ala Tyr Tyr Ser Met Ala Gly Asn Trp Ala Lys Val
                                          175
                                                               180
     Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly
                      185
          INFORMATION FOR SEQ ID NO:76:
20
     (2)
           (i)
                     SEQUENCE CHARACTERISTICS:
                          LENGTH:
                                  192 amino acids
                     (A)
                     (B)
                          TYPE:
                                 amino acid
                     (C)
                          STRANDEDNESS:
                                         unknown
                     (D)
                          TOPOLOGY:
                                    unknown
25
                     ORIGINAL SOURCE:
           (vi)
                     (A)
                          ORGANISM:
                                     homosapiens
                          INDIVIDUAL ISOLATE: US6
                     (C)
                     SEQUENCE DESCRIPTION: SEQ ID NO:76:
           (xi)
     Tyr Glu Val Arg Asn Val Ser Gly Met Tyr His Val Thr Asn Asp
30
                                           10
                                                                15
     Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Met Ile Met
     His Thr Pro Gly Cys Val Pro Cys Val Arg Glu Asn Asn Ser Ser
     Arg Cys Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Ala
     Ser Val Pro Thr Thr Thr Ile Arg Arg His Val Asp Leu Leu Val
35
                                                                75
```

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```
Gly Ala Ala Thr Phe Cys Ser Ala Met Tyr Val Gly Asp Leu Cys
                                           85
     Gly Ser Val Phe Leu Ile Ser Gln Leu Phe Thr Phe Ser Pro Arg
                       95
                                          100
     Gln His Glu Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                          115
                                                               120
     His Val Ser Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                      125
                                          130
 5
     Ser Pro Thr Ala Ala Leu Val Val Ser Gln Leu Leu Arg Ile Pro
                      140
                                          145
     Gln Ala Val Met Asp Met Val Ala Gly Ala His Trp Gly Val Leu
                      155
                                          160
     Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp Ala Lys Val
                      170
                                          175
     Leu Ile Val Leu Leu Phe Ala Gly Val Asp Gly
10
                      185
     (2)
          INFORMATION FOR SEQ ID NO:77:
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH:
                                  192 amino acids
                     (B)
                          TYPE:
                                amino acid
15
                     (C)
                          STRANDEDNESS: unknown
                     (D)
                          TOPOLOGY:
                                     unknown
          (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM:
                                     homosapiens
                     (C)
                          INDIVIDUAL ISOLATE:
20
          (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:77:
     Ala Gln Val Arg Asn Thr Ser Arg Gly Tyr Met Val Thr Asn Asp
     Cys Ser Asn Glu Ser Ile Thr Trp Gln Leu Gln Ala Ala Val Leu
                       20
                                           25
     His Val Pro Gly Cys Ile Pro Cys Glu Arg Leu Gly Asn Thr Ser
                       35
                                           40
25
     Arg Cys Trp Ile Pro Val Thr Pro Asn Val Ala Val Arg Gln Pro
                       50
                                           55
     Gly Ala Leu Thr Gln Gly Leu Arq Thr His Ile Asp Met Val Val
                       65
                                           70
     Met Ser Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys
                                                                90
     Gly Gly Val Met Leu Ala Ala Gln Met Phe Ile Val Ser Pro Arq
30
     Arg His Trp Phe Val Gln Glu Cys Asn Cys Ser Ile Tyr Pro Gly
                                                               120
     Thr Ile Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                      125
                                          130
                                                               135
     Ser Pro Thr Ala Thr Met Ile Leu Ala Tyr Ala Met Arg Val Pro
                     140
                                          145
     Glu Val Ile Ile Asp Ile Ile Gly Gly Ala His Trp Gly Val Met
35
```

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Phe Gly Leu Ala Tyr Phe Ser Met Gln Gly Ala Trp Ala Lys Val 170 175 Ile Val Ile Leu Leu Leu Ala Ala Gly Val Asp Ala INFORMATION FOR SEQ ID NO:78: (2) 5 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 192 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: unknown TOPOLOGY: unknown (D) (vi) ORIGINAL SOURCE: 10 (A) ORGANISM: homosapiens (C) INDIVIDUAL ISOLATE: T4 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:78: Ala Gln Val Lys Asn Thr Thr Asn Ser Tyr Met Val Thr Asn Asp Cys Ser Asn Asp Ser Ile Thr Trp Gln Leu Gln Ala Ala Val Leu 15 His Val Pro Gly Cys Val Pro Cys Glu Lys Thr Gly Asn Thr Ser Arg Cys Trp Ile Pro Val Ser Pro Asn Val Ala Val Arg Gln Pro Gly Ala Leu Thr Gln Gly Leu Arg Thr His Ile Asp Met Val Val 70 65 20 Met Ser Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys 80 85 90 Gly Gly Val Met Leu Ala Ala Gln Met Phe Ile Val Ser Pro Gln 105 95 100 His His Trp Phe Val Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly 110 115 120 Thr Ile Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp 125 130 25 Ser Pro Thr Ala Thr Met Ile Leu Ala Tyr Ala Met Arg Val Pro 140 145 Glu Val Ile Leu Asp Ile Val Ser Gly Ala His Trp Gly Val Met 155 160 Phe Gly Leu Ala Tyr Phe Ser Met Gln Gly Ala Trp Ala Lys Val 170 175 Val Val Ile Leu Leu Leu Ala Ala Gly Val Asp Ala 30 185 190

#### (2) INFORMATION FOR SEQ ID NO:79:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 192 amino acids
  - (B) TYPE: amino acid
- 35 (C) STRANDEDNESS: unknown

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```
TOPOLOGY: unknown
                     (D)
           (vi)
                     ORIGINAL SOURCE:
                          ORGANISM: homosapiens
                     (A)
                     (C)
                          INDIVIDUAL ISOLATE:
          (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:79:
 5
     Ala Glu Val Lys Asn Thr Ser Thr Ser Tyr Met Val Thr Asn Asp
     Cys Ser Asn Asp Ser Ile Thr Trp Gln Leu Gln Ala Ala Val Leu
     His Val Pro Gly Cys Val Pro Cys Glu Arg Val Gly Asn Ala Ser
                       35
                                           40
     Arg Cys Trp Ile Pro Val Ser Pro Asn Val Ala Val Gln Arg Pro
10
     Gly Ala Leu Thr Gln Gly Leu Arg Thr His Ile Asp Met Val Val
     Met Ser Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys
     Gly Gly Val Met Leu Ala Ala Gln Met Phe Ile Ile Ser Pro Gln
                                          100
                                                               105
     His His Trp Phe Val Gln Glu Cys Asn Cys Ser Ile Tyr Pro Gly
15
                      110
                                          115
                                                               120
     Thr Ile Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                      125
                                          130
                                                               135
     Ser Pro Thr Thr Met Ile Leu Ala Tyr Ala Met Arg Val Pro
                      140
                                          145
     Glu Val Ile Ile Asp Ile Ile Ser Gly Ala His Trp Gly Val Met
                      155
                                          160
20
     Phe Gly Leu Ala Tyr Phe Ser Met Gln Gly Ala Trp Ala Lys Val
                      170
                                          175
                                                               180
     Val Val Ile Leu Leu Thr Ala Gly Val Asp Ala
                      185
                                          190
     (2)
          INFORMATION FOR SEQ ID NO:80:
25
                    SEQUENCE CHARACTERISTICS:
          (i)
                     (A)
                         LENGTH: 192 amino acids
                     (B)
                         TYPE: amino acid
                     (C)
                          STRANDEDNESS:
                                         unknown
                     (D)
                         TOPOLOGY: unknown
                    ORIGINAL SOURCE:
          (vi)
30
                     (A)
                          ORGANISM:
                                    homosapiens
                     (C)
                          INDIVIDUAL ISOLATE: US10
          (xi)
                    SEQUENCE DESCRIPTION: SEQ ID NO:80:
     Val Gln Val Lys Asn Thr Ser Thr Ser Tyr Met Val Thr Asn Asp
     Cys Ser Asn Asp Ser Ile Thr Trp Gln Leu Glu Ala Ala Val Leu
35
```

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```
His Val Pro Gly Cys Val Pro Cys Glu Lys Val Gly Asn Thr Ser
      Arg Cys Trp Ile Pro Val Ser Pro Asn Val Ala Val Gln Arg Pro
      Gly Ala Leu Thr Gln Gly Leu Arg Thr His Ile Asp Met Val Val
                       65
     Met Ser Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Phe Cys
 5
     Gly Gly Met Met Leu Ala Ala Gln Met Phe Ile Val Ser Pro Arg
                       95
                                          100
     His His Ser Phe Val Gln Glu Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                          115
                                                               120
      Thr Ile Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                      125
                                          130
     Ser Pro Thr Ala Thr Leu Ile Leu Ala Tyr Val Met Arg Val Pro
10
                                          145
     Glu Val Ile Ile Asp Ile Ile Ser Gly Ala His Trp Gly Val Leu
                      155
     Phe Gly Leu Ala Tyr Phe Ser Met Gln Gly Ala Trp Ala Lys Val
                      170
                                          175
     Val Val Ile Leu Leu Leu Ala Ala Gly Val Asp Ala
                      185
15
      (2)
          INFORMATION FOR SEQ ID NO:81:
           (i)
                     SEOUENCE CHARACTERISTICS:
                          LENGTH: 192 amino acids
                     (A)
                          TYPE: amino acid
                     (B)
                     (C)
                          STRANDEDNESS: unknown
20
                          TOPOLOGY:
                     (D)
                                    unknown
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                          INDIVIDUAL ISOLATE: DK8
                     (C)
           (xi)
                     SEQUENCE DESCRIPTION: SEO ID NO:81:
25
     Val Glu Val Arg Asn Ile Ser Ser Ser Tyr Tyr Ala Thr Asn Asp
                                           10
     Cys Ser Asn Asn Ser Ile Thr Trp Gln Leu Thr Asp Ala Val Leu
                                           25
     His Leu Pro Gly Cys Val Pro Cys Glu Asn Asp Asn Gly Thr Leu
                                                                45
     Arg Cys Trp Ile Gln Val Thr Pro Asn Val Ala Val Lys His Arg
30
                                                                60
     Gly Ala Leu Thr His Asn Leu Arg Thr His Val Asp Val Ile Val
     Met Ala Ala Thr Val Cys Ser Ala Leu Tyr Val Gly Asp Val Cys
                                                               90
                                           85
     Gly Ala Val Met Ile Val Ser Gln Ala Leu Ile Ile Ser Pro Glu
                       95
                                          100
     Arg His Asn Phe Thr Gln Glu Cys Asn Cys Ser Ile Tyr Gln Gly
35
```

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```
His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Leu Asn Trp
                     125
                                        130
                                                             135
    Ser Pro Thr Leu Thr Met Ile Leu Ala Tyr Ala Ala Arg Val Pro
                    140
                                         145
    Glu Leu Ala Leu Gln Val Val Phe Gly Gly His Trp Gly Val Val
                    155
                                        160
    Phe Gly Leu Ala Tyr Phe Ser Met Gln Gly Ala Trp Ala Lys Val
                    170
                                        175
5
    Ile Ala Ile Leu Leu Val Ala Gly Val Asp Ala
                    185
```

### (2) INFORMATION FOR SEQ ID NO:82:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 192 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: unknown

(C) STRANDEDNESS: unknown (D) TOPOLOGY: unknown

(vi) ORIGINAL SOURCE:

(A) ORGANISM: homosapiens(C) INDIVIDUAL ISOLATE: DK1:

(C) INDIVIDUAL ISOLATE: DK11

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

Val Glu Val Arg Asn Thr Ser Ser Ser Tyr Tyr Ala Thr Asn Asp Cys Ser Asn Asn Ser Ile Thr Trp Gln Leu Thr Asn Ala Val Leu His Leu Pro Gly Cys Val Pro Cys Glu Asn Asp Asn Gly Thr Leu His Cys Trp Ile Gln Val Thr Pro Asn Val Ala Val Lys His Arg Gly Ala Leu Thr His Asn Leu Arg Ala His Ile Asp Met Ile Val Met Ala Ala Thr Val Cys Ser Ala Leu Tyr Val Gly Asp Val Cys Gly Ala Val Met Ile Val Ser Gln Ala Phe Ile Val Ser Pro Glu His His His Phe Thr Gln Glu Cys Asn Cys Ser Ile Tyr Gln Gly His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Leu Asn Trp Ser Pro Thr Leu Thr Met Ile Leu Ala Tyr Ala Ala Arg Val Pro Glu Leu Val Leu Glu Val Val Phe Gly Gly His Trp Gly Val Val Phe Gly Leu Ala Tyr Phe Ser Met Gln Gly Ala Trp Ala Lys Val Ile Ala Ile Leu Leu Leu Val Ala Gly Val Asp Ala

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```
(2)
           INFORMATION FOR SEQ ID NO:83:
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH: 192 amino acids
                          TYPE: amino acid
                     (B)
                     (C)
                          STRANDEDNESS:
                                         unknown
                          TOPOLOGY: unknown
                     (D)
 5
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE: SW3
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:83:
     Val Glu Val Arg Asn Ile Ser Ser Ser Tyr Tyr Ala Thr Asn Asp
10
                                            10
     Cys Ser Asn Ser Ser Ile Thr Trp Gln Leu Thr Asn Ala Val Leu
                       20
                                            25
     His Leu Pro Gly Cys Val Pro Cys Glu Asn Asp Asn Gly Thr Leu
                       35
                                            40
     His Cys Trp Ile Gln Val Thr Pro Asn Val Ala Val Lys His Arq
     Gly Ala Leu Thr His Asn Leu Arg Ala His Val Asp Met Ile Val
15
     Met Ala Ala Thr Val Cys Ser Ala Leu Tyr Val Gly Asp Met Cys
     Gly Ala Val Met Ile Val Ser Gln Ala Phe Ile Ile Ser Pro Glu
                                           100
     Arg His Asn Phe Thr Gln Glu Cys Asn Cys Ser Ile Tyr Gln Gly
                      110
                                          115
                                                               120
20
     Arg Ile Thr Gly His Arg Met Ala Trp Asp Met Met Leu Asn Trp
                      125
                                          130
                                                               135
     Ser Pro Thr Leu Thr Met Ile Leu Ala Tyr Ala Ala Arg Val Pro
                      140
                                          145
     Glu Leu Val Leu Glu Val Val Phe Gly Gly His Trp Gly Val Val
                      155
                                          160
     Phe Gly Leu Ala Tyr Phe Ser Met Gln Gly Ala Trp Ala Lys Val
                      170
                                          175
                                                               180
25
     Ile Ala Ile Leu Leu Leu Val Ala Gly Val Asp Ala
                      185
                                          190
     (2)
          INFORMATION FOR SEQ ID NO:84:
           (i)
                     SEQUENCE CHARACTERISTICS:
30
                          LENGTH: 192 amino acids
                     (A)
                          TYPE:
                                 amino acid
                     (B)
                     (C)
                          STRANDEDNESS: unknown
                     (D)
                          TOPOLOGY:
                                     unknown
          (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                          INDIVIDUAL ISOLATE: T8
                     (C)
35
```

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```
0
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:84:
     Val Glu Val Arg Asn Thr Ser Phe Ser Tyr Tyr Ala Thr Asn Asp
      Cys Ser Asn Asn Ser Ile Thr Trp Gln Leu Thr Asn Ala Val Leu
                                            25
     His Leu Pro Gly Cys Val Pro Cys Glu Asn Asp Asn Gly Thr Leu
 5
     Arg Cys Trp Ile Gln Val Thr Pro Asn Val Ala Val Lys His Arg
                                            55
     Gly Ala Leu Thr His Asn Leu Arg Thr His Val Asp Val Ile Val
                                            70
     Met Ala Ala Thr Val Cys Ser Ala Leu Tyr Val Gly Asp Val Cys
                       80
                                            85
     Gly Ala Val Met Ile Ala Ser Gln Ala Phe Ile Ile Ser Pro Glu
10
                       95
                                           100
     Arg His Asn Phe Thr Gln Glu Cys Asn Cys Ser Ile Tyr Gln Gly
                      110
                                           115
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Leu Asn Trp
                      110
                                           115
                                                               120
     Ser Pro Thr Leu Thr Met Ile Leu Ala Tyr Ala Ala Arg Val Pro
                      125
     Glu Leu Val Leu Glu Val Val Phe Gly Gly His Trp Gly Val Val
15
                      140
     Phe Gly Leu Ala Tyr Phe Ser Met Gln Gly Ala Trp Ala Lys Val
                      155
     Ile Ala Ile Leu Leu Leu Val Ala Gly Val Asp Ala
                      170
20
     (2)
          INFORMATION FOR SEQ ID NO:85:
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH:
                                  192 amino acids
                     (B)
                          TYPE: amino acid
                     (C)
                          STRANDEDNESS:
                                         unknown
                     (D)
                          TOPOLOGY:
                                    unknown
25
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                          INDIVIDUAL ISOLATE:
                     (C)
                     SEQUENCE DESCRIPTION: SEQ ID NO:85:
           (xi)
     Val Glu Val Lys Asp Thr Gly Asp Ser Tyr Met Pro Thr Asn Asp
30
                                           10
     Cys Ser Asn Ser Ser Ile Val Trp Gln Leu Glu Gly Ala Val Leu
                       20
     His Thr Pro Gly Cys Val Pro Cys Glu Arg Thr Ala Asn Val Ser
     Arg Cys Trp Val Pro Val Ala Pro Asn Leu Ala Ile Ser Gln Pro
     Gly Ala Leu Thr Lys Gly Leu Arg Ala His Ile Asp Ile Ile Val
35
```

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```
Met Ser Ala Thr Val Cys Ser Ala Leu Tyr Val Gly Asp Val Cys
                                           85
                                                                90
     Gly Ala Leu Met Leu Ala Ala Gln Val Val Val Ser Pro Gln
                                          100
     His His Thr Phe Val Gln Glu Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                          115
                                                               120
     Arg Ile Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                      125
                                          130
 5
     Ser Pro Thr Thr Met Leu Leu Ala Tyr Leu Val Arg Ile Pro
                      140
                                          145
                                                               150
     Glu Val Ile Leu Asp Ile Val Thr Gly Gly His Trp Gly Val Met
                      155
                                          160
     Phe Gly Leu Ala Tyr Phe Ser Met Gln Gly Ser Trp Ala Lys Val
                      170
                                          175
     Ile Val Ile Leu Leu Leu Thr Ala Gly Val Glu Ala
10
     (2)
          INFORMATION FOR SEQ ID NO:86:
           (i)
                     SEQUENCE CHARACTERISTICS:
                          LENGTH:
                                   192 amino acids
                     (B)
                          TYPE:
                                 amino acid
15
                     (C)
                          STRANDEDNESS: unknown
                     (D)
                          TOPOLOGY: unknown
           (vi)
                     ORIGINAL SOURCE:
                          ORGANISM: homosapiens
                          INDIVIDUAL ISOLATE:
                                              DK12
20
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:86:
     Leu Glu Trp Arg Asn Val Ser Gly Leu Tyr Val Leu Thr Asn Asp
     Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val Ile Leu
     His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr Ser
                                           40
25
     Thr Cys Trp Thr Ser Val Thr Pro Thr Val Ala Val Arg Tyr Val
                       50
                                           55
     Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val
                       65
                                           70
     Gly Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Val Cys
                                           85
     Gly Ala Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg
30
                       95
                                          100
                                                              105
     Arg His Gln Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly
                      110
                                          115
     His Leu Ser Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                                          130
                                                              135
     Ser Pro Ala Val Gly Met Val Val Ala His Val Leu Arg Leu Pro
                      140
     Gln Thr Leu Phe Asp Ile Ile Ala Gly Ala His Trp Gly Ile Met
35
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Ala Gly Leu Ala Tyr Tyr Ser Met Gln Gly Asn Trp Ala Lys Val 170 175 Ala Ile Ile Met Val Met Phe Ser Gly Val Asp Ala 185 (2). INFORMATION FOR SEQ ID NO:87: 5 (i)SEQUENCE CHARACTERISTICS: (A) LENGTH: 192 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: unknown (D) TOPOLOGY: unknown (vi) ORIGINAL SOURCE: 10 (A) ORGANISM: homosapiens (C) INDIVIDUAL ISOLATE: HK10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:87: Leu Glu Trp Arg Asn Val Ser Gly Leu Tyr Val Leu Thr Asn Asp Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val Ile Leu 15 His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr Ser 35 Thr Cys Trp Thr Ser Val Thr Pro Thr Val Ala Val Arg Tyr Val 55 60 Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val 70 75 Gly Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys 20 80 85 90 Gly Ala Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg 95 100 105 Arg His Gln Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly 110 115 120 His Leu Ser Gly His Arg Met Ala Trp Asp Met Met Asn Trp 125 130 135 25 Ser Pro Ala Val Gly Met Val Val Ala His Val Leu Arg Leu Pro 140 145 Gln Thr Leu Phe Asp Ile Ile Ala Gly Ala His Trp Gly Ile Leu 155 160 Ala Gly Leu Ala Tyr Tyr Ser Met Gln Gly Asn Trp Ala Lys Val 170 175

#### (2) INFORMATION FOR SEQ ID NO:88:

185

30

SEQUENCE CHARACTERISTICS: (i)

Ala Ile Ile Met Val Met Phe Ser Gly Val Asp Ala

- (A) LENGTH: 192 amino acids
- (B) TYPE: amino acid
- 35 (C) STRANDEDNESS: unknown

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(D) TOPOLOGY: unknown (vi) ORIGINAL SOURCE: ORGANISM: homosapiens (A) (C) INDIVIDUAL ISOLATE: SEQUENCE DESCRIPTION: SEQ ID NO:88: (xi) 5 Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val Ile Leu 20 25 His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr Ser 35 40 Thr Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr Val 10 Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val Gly Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly Ala Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg 100 105 Arg His Gln Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly 15 120 110 115 His Leu Ser Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp 130 135 125 Ser Pro Ala Val Gly Met Val Val Ala His Val Leu Arg Leu Pro 140 145 Gln Thr Val Phe Asp Ile Ile Ala Gly Ala His Trp Gly Ile Leu 155 160 20 Ala Gly Leu Ala Tyr Tyr Ser Met Gln Gly Asn Trp Ala Lys Val 170 175 Ala Ile Ile Met Val Met Phe Ser Gly Val Asp Ala 185 190 (2) INFORMATION FOR SEQ ID NO:89: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 192 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: unknown TOPOLOGY: unknown (vi) ORIGINAL SOURCE: 30 (A) ORGANISM: homosapiens (C) INDIVIDUAL ISOLATE: (xi) SEQUENCE DESCRIPTION: SEQ ID NO:89: Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu Thr Asn Asp 10 Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val Ile Leu 35

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```
His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr Ser
      Met Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr Val
      Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val
                                                                75
      Gly Ala Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Met Cys
                                            85
                                                                 90
 5
     Gly Ala Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg
                       95
                                           100
                                                                105
     Arg His Gln Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly
                      110
                                           115
                                                                120
     His Val Ser Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                      125
                                           130
     Ser Pro Ala Val Gly Met Val Val Ala His Ile Leu Arg Leu Pro
10
                      140
                                           145
     Gln Thr Leu Phe Asp Ile Leu Ala Gly Ala His Trp Gly Ile Leu
                      155
                                           160
     Ala Gly Leu Ala Tyr Tyr Ser Met Gln Gly Asn Trp Ala Lys Val
                      170
                                           175
     Ala Ile Val Met Ile Met Phe Ser Gly Val Asp Ala
15
           INFORMATION FOR SEQ ID NO:90:
      (2)
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH:
                                   192 amino acids
                     (B)
                          TYPE:
                                amino acid
                          STRANDEDNESS: unknown
                     (C)
20
                          TOPOLOGY:
                                    unknown
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM:
                                     homosapiens
                     (C)
                          INDIVIDUAL ISOLATE:
                     SEQUENCE DESCRIPTION: SEQ ID NO:90:
           (xi)
25
     Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Ile Leu Thr Asn Asp
     Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val Ile Leu
                       20
     His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr Ser
                       35
                                           40
     Thr Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr Val
30
                       50
                                           55
     Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val
                       65
                                           70
                                                                75
     Gly Ala Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Met Cys
                       80
                                           85
     Gly Ala Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg
     Arg His Gln Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly
35
                      110
                                                               120
```

10

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#### (2) INFORMATION FOR SEQ ID NO:91:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 192 amino acids

(B) TYPE: amino acid

- (C) STRANDEDNESS: unknown
- (D) TOPOLOGY: unknown
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: homosapiens
  - (C) INDIVIDUAL ISOLATE: Z4
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

```
Glu His Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp
     Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp His His Ile Leu
     His Leu Pro Gly Cys Val Pro Cys Val Met Thr Gly Asn Thr Ser
20
     Arg Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Ala His Pro
                      50
     Gly Ala Pro Leu Glu Ser Phe Arg Arg His Val Asp Leu Met Val
                                                               75
     Gly Ala Ala Thr Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys
                                                               90
                      80
                                          85
25
     Gly Gly Ala Phe Leu Met Gly Gln Met Ile Thr Phe Arg Pro Arg
                                                              105
                                         100
                      95
     Arg His Trp Thr Thr Gln Glu Cys Asn Cys Ser Ile Tyr Thr Gly
                                         115
                     110
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                                                              135
                                         130
                     125
     Ser Pro Thr Thr Leu Leu Leu Ala Gln Ile Met Arg Val Pro
30
                     140
                                         145
                                                              150
     Thr Ala Phe Leu Asp Met Val Ala Gly Gly His Trp Gly Val Leu
                                         160
                     155
     Ala Gly Leu Ala Tyr Phe Ser Met Gln Gly Asn Trp Ala Lys Val
                     170
                                         175
     Val Leu Val Leu Phe Leu Phe Ala Gly Val Asp Ala
```

35

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```
INFORMATION FOR SEQ ID NO:92:
      (2)
           (i)
                     SEQUENCE CHARACTERISTICS:
                          LENGTH: 192 amino acids
                     (A)
                          TYPE: amino acid
                      (B)
                     (C)
                          STRANDEDNESS: unknown
                          TOPOLOGY: unknown
                     (D)
 5
           (vi)
                     ORIGINAL SOURCE:
                          ORGANISM: homosapiens
                     (A)
                     (C)
                          INDIVIDUAL ISOLATE:
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:92:
     Val His Tyr Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp
10
     Cys Pro Asn Thr Ser Ile Val Tyr Glu Thr Glu His His Ile Met
     His Leu Pro Gly Cys Val Pro Cys Val Arg Thr Glu Asn Thr Ser
     Arg Cys Trp Val Pro Leu Thr Pro Thr Val Ala Ala Pro Tyr Pro
     Asn Ala Pro Leu Glu Ser Met Arg Arg His Val Asp Leu Met Val
15
                                           70
     Gly Ala Ala Thr Met Cys Ser Ala Phe Tyr Ile Gly Asp Leu Cys
                       80
     Gly Gly Val Phe Leu Val Gly Gln Leu Phe Asp Phe Arg Pro Arg
                                          100
                                                               105
     Arg His Trp Thr Thr Gln Asp Cys Asn Cys Ser Ile Tyr Pro Gly
                      110
                                          115
20
     His Val Ser Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                      125
                                          130
     Ser Pro Thr Ser Ala Leu Ile Met Ala Gln Ile Leu Arg Ile Pro
                      140
                                          145
     Ser Ile Leu Gly Asp Leu Leu Thr Gly Gly His Trp Gly Val Leu
                      155
                                          160
     Ala Gly Leu Ala Phe Phe Ser Met Gln Ser Asn Trp Ala Lys Val
                      170
                                          175
25 -
     Ile Leu Val Leu Phe Leu Phe Ala Gly Val Glu Gly
                      185
                                          190
     (2)
          INFORMATION FOR SEQ ID NO:93:
           (i)
                     SEQUENCE CHARACTERISTICS:
30
                     (A)
                          LENGTH: 192 amino acids
                     (B)
                          TYPE: amino acid
                          STRANDEDNESS:
                     (C)
                          TOPOLOGY: unknown
          (vi)
                     ORIGINAL SOURCE:
                          ORGANISM: homosapiens
                     (A)
                     (C)
                          INDIVIDUAL ISOLATE: Z6
35
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```
(xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:93:
     Val Asn Tyr Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp
     Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Glu His Gln Ile Leu
     His Leu Pro Gly Cys Leu Pro Cys Val Arg Val Gly Asn Gln Ser
     Arg Cys Trp Val Ala Leu Thr Pro Thr Val Ala Val Ser Tyr Ile
     Gly Ala Pro Leu Asp Ser Leu Arg Arg His Val Asp Leu Met Val
                       65
     Gly Ala Ala Thr Val Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys
                       80
                                           85
     Gly Gly Ala Phe Leu Val Gly Gln Met Phe Ser Phe Gln Pro Arg
10
                                          100
     Arg His Trp Thr Thr Gln Asp Cys Asn Cys Ser Ile Tyr Ala Gly
                      110
                                          115
                                                               120
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                      125
                                          130
                                                               135
     Ser Pro Thr Thr Leu Leu Leu Ala Gln Val Met Arg Ile Pro
                      140
                                          145
     Ser Thr Leu Val Asp Leu Leu Ala Gly Gly His Trp Gly Val Leu
15
                      155
                                          160
     Val Gly Leu Ala Tyr Phe Ser Met Gln Ala Asn Trp Ala Lys Val
                                          175
                      170
                                                               180
     Ile Leu Val Leu Phe Leu Phe Ala Gly Val Asp Ala
                      185
                                          190
     (2)
          INFORMATION FOR SEQ ID NO:94:
20
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH: 192 amino acids
                     (B)
                          TYPE: amino acid
                     (C)
                          STRANDEDNESS:
                                         unknown
                     (D)
                          TOPOLOGY: unknown
           (vi)
                     ORIGINAL SOURCE:
25
                          ORGANISM: homosapiens
                     (A)
                          INDIVIDUAL ISOLATE:
                     (C)
                     SEQUENCE DESCRIPTION: SEQ ID NO:94:
           (xi)
     Val Asn Tyr His Asn Ala Ser Gly Val Tyr His Ile Thr Asn Asp
30
     Cys Pro Asn Ser Ser Ile Met Tyr Glu Ala Glu His His Ile Leu
                       20
                                           25
     His Leu Pro Gly Cys Val Pro Cys Val Arg Glu Gly Asn Gln Ser
                       35
                                           40
     Arg Cys Trp Val Ala Leu Thr Pro Thr Val Ala Ala Pro Tyr Ile
     Gly Ala Pro Leu Glu Ser Ile Arg Arg His Val Asp Leu Met Val
35
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Gly Ala Ala Thr Val Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys
                                            85
                                                                90
      Gly Gly Val Phe Leu Val Gly Gln Met Phe Ser Phe Gln Pro Arg
                       95
                                           100
                                                               105
     Arg His Trp Thr Thr Gln Asp Cys Asn Cys Ser Ile Tyr Ala Gly
                      110
                                           115
                                                               120
      His Val Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                      125
 5
                                          130
      Ser Pro Thr Thr Leu Val Leu Ala Gln Val Met Arg Ile Pro
                      140
                                           145
                                                               150
      Ser Thr Leu Val Asp Leu Leu Thr Gly Gly His Trp Gly Ile Leu
                      155
                                          160
      Ile Gly Val Ala Tyr Phe Cys Met Gln Ala Asn Trp Ala Lys Val
                      170
                                          175
      Ile Leu Val Leu Phe Leu Tyr Ala Gly Val Asp Ala
10
      (2)
          INFORMATION FOR SEQ ID NO:95:
           (i)
                     SEQUENCE CHARACTERISTICS:
                     (A)
                          LENGTH: 192 amino acids
                     (B)
                          TYPE: amino acid
15
                          STRANDEDNESS: unknown
                     (C)
                     (D)
                          TOPOLOGY:
                                     unknown
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE: DK13
20
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:95:
     Tyr Asn Tyr Arg Asn Ser Ser Gly Val Tyr His Val Thr Asn Asp
     Cys Pro Asn Ser Ser Ile Val Tyr Glu Thr Asp Tyr His Ile Leu
                       20
                                           25
     His Leu Pro Gly Cys Val Pro Cys Val Arg Glu Gly Asn Lys Ser
                                           40
25
     Thr Cys Trp Val Ser Leu Thr Pro Thr Val Ala Ala Gln His Leu
                       50
                                           55
     Asn Ala Pro Leu Glu Ser Leu Arg Arg His Val Asp Leu Met Val
                       65
                                           70
     Gly Gly Ala Thr Leu Cys Ser Ala Leu Tyr Ile Gly Asp Val Cys
                       80
                                           85
                                                                90
     Gly Gly Val Phe Leu Val Gly Gln Leu Phe Thr Phe Gln Pro Arg
30
                                                               105
     Arg His Trp Thr Thr Gln Asp Cys Asn Cys Ser Ile Tyr Thr Gly
                                                               120
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                                                               135
     Ser Pro Thr Ala Thr Leu Val Leu Ala Gln Leu Met Arg Ile Pro
                      140
                                          145
     Gly Ala Met Val Asp Leu Leu Ala Gly Gly His Trp Gly Ile Leu
35
```

160

155

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Val Gly Ile Ala Tyr Phe Ser Met Gln Ala Asn Trp Ala Lys Val-170 175 Ile Leu Val Leu Phe Leu Phe Ala Gly Val Asp Ala 185 (2) INFORMATION FOR SEQ ID NO:96: (i) SEQUENCE CHARACTERISTICS: 5 (A) LENGTH: 192 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: unknown (D) TOPOLOGY: unknown (vi) ORIGINAL SOURCE: (A) ORGANISM: homosapiens 10 INDIVIDUAL ISOLATE: SA1 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:96: Val Pro Tyr Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp 10 Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Ser Leu Ile Leu 15 His Ala Pro Gly Cys Val Pro Cys Val Arg Gln Asp Asn Val Ser 35 40 Arg Cys Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Thr Phe Gly Ala Val Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala 75 Gly Gly Ala Ala Leu Cys Ser Ala Leu Tyr Val Gly Asp Ala Cys 20 90 Gly Ala Val Phe Leu Val Gly Gln Met Phe Thr Tyr Arg Pro Arg 95 100 105 Gln His Thr Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Ser Gly 110 115 120 His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp 125 130 Ser Pro Thr Thr Ala Leu Leu Met Ala Gln Met Leu Arg Ile Pro 25 140 145 Gln Val Val Ile Asp Ile Ile Ala Gly Gly His Trp Gly Val Leu 155 160 Phe Ala Ala Ala Tyr Phe Ala Ser Ala Ala Asn Trp Ala Lys Val 170 175 Val Leu Val Leu Phe Leu Phe Ala Gly Val Asp Gly 185 30 (2) INFORMATION FOR SEQ ID NO:97: (i)SEQUENCE CHARACTERISTICS: 192 amino acids LENGTH: (B) TYPE: amino acid

STRANDEDNESS: unknown

TOPOLOGY: unknown

(C)

(D)

35

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(vi) ORIGINAL SOURCE: ORGANISM: homosapiens (A) INDIVIDUAL ISOLATE: SA4 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:97: Val Pro Tyr Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp 5 Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu 25 His Ala Pro Gly Cys Val Pro Cys Val Arg Gln Asp Asn Val Ser 35 Lys Cys Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Asn Leu 50 55 Gly Ala Val Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala 10 65 70 Gly Gly Ala Ala Leu Cys Ser Ala Leu Tyr Val Gly Asp Ala Cys 80 90 Gly Ala Val Phe Leu Val Gly Gln Met Phe Thr Tyr Arg Pro Arg 95 Gln His Thr Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Ser Gly 110 120 His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp 15 135 Ser Pro Thr Thr Ala Leu Leu Met Ala Gln Leu Leu Arg Ile Pro 145 Gln Val Val Ile Asp Ile Ile Ala Gly Gly His Trp Gly Val Leu 155 160 Phe Ala Ala Ala Tyr Phe Ala Ser Ala Ala Asn Trp Ala Lys Val 170 175 20 Ile Leu Val Leu Phe Leu Phe Ala Gly Val Asp Ala 185 (2) INFORMATION FOR SEQ ID NO:98: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 192 amino acids 25 (B) TYPE: amino acid (C) STRANDEDNESS: unknown (D) TOPOLOGY: unknown (vi) ORIGINAL SOURCE: (A) ORGANISM: homosapiens (C) INDIVIDUAL ISOLATE: 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:98: Val Pro Tyr Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His Ala Pro Gly Cys Val Pro Cys Val Lys Glu Gly Asn Val Ser 35

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```
Arg Cys Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Asn Leu
     Gly Ala Val Thr Ala Pro Leu Arg Arg Val Val Asp Tyr Leu Ala
                                                                75
                       65
     Gly Gly Ala Ala Leu Cys Ser Ala Leu Tyr Val Gly Asp Ala Cys
                                                                90
                                           85
                       80
     Gly Ala Val Phe Leu Val Gly Gln Met Phe Thr Tyr Arg Pro Arg
                                                               105
                                          100
                       95
 5
     Gln His Thr Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Ser Gly
                                          115
                                                               120
                      110
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                                          130
                                                               135
                      125
     Ser Pro Thr Thr Ala Leu Val Met Ala Gln Val Leu Arg Ile Pro
                      140
                                          145
     Gln Val Val Ile Asp Ile Ile Ala Gly Gly His Trp Gly Val Leu
10
                                          160
                      155
     Phe Ala Val Ala Tyr Phe Ala Ser Ala Ala Asn Trp Ala Lys Val
                      170
                                          175
     Val Leu Val Leu Phe Leu Phe Ala Gly Val Asp Gly
          INFORMATION FOR SEQ ID NO:99:
     (2)
15
                     SEQUENCE CHARACTERISTICS:
          (i)
                     (A)
                          LENGTH:
                                  192 amino acids
                     (B)
                          TYPE: amino acid
                     (C)
                          STRANDEDNESS: unknown
                          TOPOLOGY:
                     (D)
                                    unknown
20
          (vi)
                     ORIGINAL SOURCE:
                          ORGANISM: homosapiens
                     (A)
                     (C)
                          INDIVIDUAL ISOLATE:
           (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:99:
     Val Pro Tyr Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp
25
     Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Leu Ile Leu
                       20
                                           25
     His Ala Pro Gly Cys Val Pro Cys Val Arg Lys Asp Asn Val Ser
                                           40
     Arg Cys Trp Val His Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu
                       50
                                           55
     Gly Ala Val Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala
                                           70
                       65
30
     Gly Gly Ala Ala Leu Cys Ser Ala Leu Tyr Val Gly Asp Val Cys
                       80
                                           85
     Gly Ala Leu Phe Leu Val Gly Gln Met Phe Thr Tyr Arg Pro Arg
     Gln His Ala Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Ser Gly
                                          115
                                                               120
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
35
                                          130
                                                               135
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```
Ser Pro Ala Thr Ala Leu Val Met Ala Gln Met Leu Arg Ile Pro
                                           145
     Gln Val Val Ile Asp Ile Ile Ala Gly Gly His Trp Gly Val Leu
                      155
                                           160
                                                               165
     Phe Ala Ala Ala Tyr Phe Ala Ser Ala Ala Asn Trp Ala Lys Val
                      170
                                           175
     Val Leu Val Leu Phe Leu Phe Ala Gly Val Asp Ala
                      185
 5
     (2)
          INFORMATION FOR SEQ ID NO:100:
           (i)
                     SEQUENCE CHARACTERISTICS:
                          LENGTH:
                                   192 amino acids
                     (B)
                          TYPE:
                                 amino acid
10
                     (C)
                          STRANDEDNESS: unknown
                     (D)
                          TOPOLOGY:
                                    unknown
           (vi)
                     ORIGINAL SOURCE:
                     (A)
                          ORGANISM:
                                     homosapiens
                     (C)
                          INDIVIDUAL ISOLATE:
          (xi)
                     SEQUENCE DESCRIPTION: SEQ ID NO:100:
15
     Val Pro Tyr Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp
     Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu
                       20
                                           25
     His Ala Pro Gly Cys Val Pro Cys Val Arg Gln Asn Asn Val Ser
                       35
                                           40
20
     Arg Cys Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Asn Leu
                       50
                                           55
     Gly Ala Val Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala
                       65
                                           70
                                                                75
     Gly Gly Ala Ala Leu Cys Ser Ala Leu Tyr Val Gly Asp Ala Cys
                       80
                                           85
     Gly Ala Val Phe Leu Val Gly Gln Met Phe Ser Tyr Arg Pro Arg
                       95
                                          100
25
     Gln His Thr Thr Val Gln Asp Cys Asn Cys Ser Ile Tyr Ser Gly
                      110
                                          115
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Asn Trp
                      125
                                          130
     Ser Pro Thr Thr Ala Leu Val Met Ala Gln Leu Leu Arg Ile Pro
                      140
                                          145
     Gln Val Val Ile Asp Ile Ile Ala Gly Gly His Trp Gly Val Leu
30
                      155
                                          160
```

Phe Ala Ala Ala Tyr Phe Ala Ser Ala Ala Asn Trp Ala Lys Val

(2) INFORMATION FOR SEQ ID NO:101:

35

170

185

Val Leu Val Leu Phe Leu Phe Ala Gly Val Asp Ala

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```
(i)
                     SEQUENCE CHARACTERISTICS:
                          LENGTH: 192 amino acids
                     (A)
                     (B)
                          TYPE: amino acid
                     (C)
                          STRANDEDNESS: unknown
                     (D)
                          TOPOLOGY: unknown
          (vi)
                     ORIGINAL SOURCE:
                          ORGANISM: homosapiens
                     (A)
 5
                          INDIVIDUAL ISOLATE: SA13
                     (C)
          (xi)
                    SEQUENCE DESCRIPTION: SEQ ID NO:101:
     Val Pro Tyr Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp
     Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Leu Ile Leu
10
                       20
                                           25
     His Ala Pro Gly Cys Val Pro Cys Val Arg Gln Gly Asn Val Ser
                       35
                                           40
     Arg Cys Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu
     Gly Ala Val Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala
     Gly Gly Ala Ala Leu Cys Ser Ala Leu Tyr Val Gly Asp Ala Cys
15
                                                                90
     Gly Ala Val Phe Leu Val Gly Gln Met Phe Thr Tyr Ser Pro Arg
                                                               105
     Arg His Asn Val Val Gln Asp Cys Asn Cys Ser Ile Tyr Ser Gly
                                                               120
     His Ile Thr Gly His Arg Met Ala Trp Asp Met Met Met Asn Trp
                      125
                                          130
                                                               135
     Ser Pro Thr Thr Ala Leu Val Met Ala Gln Leu Leu Arg Ile Pro
20
                      140
                                          145
     Gln Val Val Ile Asp Ile Ile Ala Gly Ala His Trp Gly Val Leu
                      155
                                          160
     Phe Ala Ala Ala Tyr Tyr Ala Ser Ala Ala Asn Trp Ala Lys Val
                      170
                                          175
     Val Leu Val Leu Phe Leu Phe Ala Gly Val Asp Ala
                                          190
                      185
25
     (2)
          INFORMATION FOR SEQ ID NO:102:
                    SEQUENCE CHARACTERISTICS:
          (i)
                     (A)
                          LENGTH: 192 amino acids
                          TYPE: amino acid
                     (B)
                          STRANDEDNESS: unknown
30
                     (C)
                          TOPOLOGY: unknown
          (vi)
                    ORIGINAL SOURCE:
                     (A)
                          ORGANISM: homosapiens
                     (C)
                          INDIVIDUAL ISOLATE: HK2
                    SEQUENCE DESCRIPTION: SEQ ID NO:102:
          (xi)
35
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•	Leu	Thr	Tyr	Gln	Asn	Ser	Ser	Gln	Leu	Tyr	His	Leu	Thr	Asn	Asp
	Cvs	Pro	Asn	Ser	1 Ser	Ile	Val	Leu	Glu	10 Ala	Asp	Ala	Met	Ile	15 Len
	_				20					25	_				30
	His	Leu	Pro	GIN	Cys 35	Leu	Pro	Cys	Val	Arg 40	Val	Asp	Asp	Arg	Ser 45
_	Thr	Cys	Trp	His	Ala 50	Val	Thr	Pro	Thr	Leu 55	Ala	Ile	Pro	Asn	
5	Ser	Thr	Pro	Ala	Thr 65	Gln	Phe	Arg	Arg		Val	Asp	Leu	Leu	60 Ala 75
•	Gln	Ala	Ala	Val	Val 80	Cys	Ser	Ser	Leu	Tyr 85	Ile	Gln	Asp	Leu	Cys 90
	Gln	Ser	Leu	Phe	Leu 95	Ala	Gln	Gln	Leu		Thr	Phe	Gln	Pro	
10	Arg	His	Trp	Thr	Val 110	Gln	Asp	Cys	Asn	Cys 115	Ser	Ile	Tyr	Thr	Gln 120
	His	Val	Thr	Gln	His 125	Arg	Met	Ala	Trp	Asp	Met	Met	Met	Asn	
	Ser	Pro	Thr	Thr	Thr 140	Leu	Val	Leu	Ser		Ile	Leu	Arg	Val	Pro
	Glu	Ile	Cys	Ala	Ser	Val	Ile	Phe	Gln	Gln	His	Trp	Gln	Ile	
15	Leu	Ala	Val	Ala	155 Tyr	Phe	Gln	Met	Ala		Asn	Trp	Leu	Lys	
	Leu	Ala	Val	Leu	170 Phe 185	Leu	Phe	Ala	Gln	175 Val 190	Glu	Ala			180
	(2)	INI	FORM	TION	v FOR	SEÇ	Q ID	NO:1	.03:						
		(i)	)	٤	SEQUE	ENCE	CHAF	LACTE	RIST	CICS:					
20		,_,	,	1	(A)	LENG	ETH:	40 k	ase	pair					
				1	(C)		ANDEI	ucle NESS	: s	singl	.e				
				ı	(D)	TOPO	DLOG	r: 1	inea	ır					
		(xi	i)	S	SEQUE	ENCE	DESC	RIPT	NOI:	SEC	ID	NO:1	.03:		
25	GCGT	rccgo	GT 1	CTG	BAAGA	C GG	CGT	AACT	OTA '	CAAC	AGG				40
	(2)	INI	FORM	TIOI	I FOR	SEÇ	) ID	NO:1	.04:						
		(i)	)		SEQUE	LENG	TH:	40 b	ase	pair					
30				(	(B) (C) (D)	TYPE	E: r	ucle NESS	ic a	cid ingl					
•		( <b>x</b> :	L)	S	SEQUE	NCE	DESC	RIPI	'ION:	SEÇ	ID	NO:1	.04:		
	AGG	CTTTC	CAT 1	rgcac	STTCA	A GO	CCGI	GCTA	TTG	ATGI	GCC				40

35 (2) INFORMATION FOR SEQ ID NO:105:

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•		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 40 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:105:	
5	AAGA	.CGGCGT GA	ACTATGCA ACAGGGAACC TTCCTGGTTG	40
	(2)	INFORMAT	ION FOR SEQ ID NO:106:	
10		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 40 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:106:	
	AGTT	CAAGGC CG	TGCTATTG ATGTGCCAAC TGCCGTTGGT	40
15	(2)	INFORMAT	ION FOR SEQ ID NO:107:	
20		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 40 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:107:	
	AAGA	CGGCGT GA	ATTCTGCA ACAGGGAACC TTCCTGGTTG	40
25	(2)	INFORMAT	ION FOR SEQ ID NO:108:	
		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 40 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
30		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:108:	
	AGTT	'CAAGGC CG'	TGGAATTC ATGTGCCAAC TGCCGTTGGT	40
	(2)	INFORMAT	ION FOR SEQ ID NO:109:	
35		(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 42 base pairs	

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J			<ul><li>(B) TYPE: nucleic acid</li><li>(C) STRANDEDNESS: single</li><li>(D) TOPOLOGY: linear</li></ul>	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:109:	
5	ARCT	YCGACG T	VACATCGAY CTGCTYGTYG GRAGYGCCAC CC	42
	(2)	INFORMAT	FION FOR SEQ ID NO:110:	
10		(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:110:	
	RCAR	GCCRTC T	TGGAYATGA TCGCTGGWGC Y	31
15	(2)	INFORMAT	TION FOR SEQ ID NO:111:	
		(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 42 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
20		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:111:	
	CRAT	ACGACR YO	CAYGTCGAY TTGCTCGTTG GGGCGGCTRY YT	42
	(2)	INFORMAT	TION FOR SEQ ID NO:112:	
25		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 31 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:112:	
30	RCAA	GCTRTC RT	GGAYRTGG TRRCRGGRGC C	31
	(2)	INFORMAT	TION FOR SEQ ID NO:113:	
35		(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 40 base pairs (B) TYPE: nucleic acid	
23			(C) STRANDEDNESS: single	

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•		,	(D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:113:	
	TTGC	GGACKC ACA	ATYGACAT GGTYGTGATG TCCGCCACGC	40
5	(2)	INFORMATI	CON FOR SEQ ID NO:114:	
		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 43 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
10		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:114:	
	GATG	CGCGTT CCC	CGAGGTCA TCWTAGACAT CRTYRGCGGR GCD	43
	(2)	INFORMATI	ON FOR SEQ ID NO:115:	
15		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 54 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:115:	
20	AATG		CRCTGCTG GATACAAGTR ACACCTAATG TGGCTGTGAA	50 54
	(2)	INFORMATI	CON FOR SEQ ID NO:116:	
25		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 31 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:116:	
30	ARCT	AGYC CTYSA	ARGTYG TCTTCGGYGG Y	31
	(2)	INFORMATI	ON FOR SEQ ID NO:117:	
		(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 54 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single	
35			(C) SIRANDEDNESS: SINGLE (D) TOPOLOGY: linear	

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•		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:117:	
	GCCA TCAA		CGATGTTG GGTGCCGGTT GCCCCCAATC TCGCCATAAG	50 54
	(2).	INFORMAT	ION FOR SEQ ID NO:118:	
5		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 46 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
10		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:118:	
	AAGG	GCCTGC GAG	GCACACAT CGATATCATC GTGATGTCTG CTACGG	46
	(2)	INFORMATI	ION FOR SEQ ID NO:119:	
15		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 45 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:119:	
20	TTGG	TGCGCA TCC	CCGGAAGT CATCTTGGAT ATTGTTACAG GAGGT	45
	(2)	INFORMATI	ON FOR SEQ ID NO:120:	
25		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 40 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:120:	
	AGTC	AGGTAY GTO	CGGAGCAA CCACCGCYTC GATACGCAGT	40
30	(2)	INFORMATI	ON FOR SEQ ID NO:121:	
		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 46 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
35		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:121:	

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	AGCC	TTCACG	TTCAGACCKC GTCGCCATCA AACRGTCCAG ACCTGT	46
	(2)	INFORM	MATION FOR SEQ ID NO:122:	
5		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 75 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:122:	
10			TGGGTATGGT GGTRGCGCAC RTYCTGCGDY TGCCCCAGAC ATAMTRGCYG GGGCC	50 75
	(2)	INFOR	MATION FOR SEQ ID NO:123:	
15		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 39 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:123:	
	ACGC	CGGTGA	CGCCTACAGT GGCTGTCGCA CACCCGGGC	39
20	(2)	INFOR	MATION FOR SEQ ID NO:124:	
		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 42 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
25		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:124:	
	ATGA	GGGTCC	CCACAGCCTT TCTCGACATG GTTGCCGGAG GC	42
	(2)	INFORM	MATION FOR SEQ ID NO:125:	
30		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 40 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:125:	
35	CGCG	CCCTAT	CCCAACGCAC CGTTAGAGTC CATGCGCAGG	40

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	(2)	INFORMAT	ION FOR SEQ ID NO:126:	
5		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 49 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:126:	
	TCAG	ATCTTA CG	GATCCCCT CTATCCTAGG TGACTTGCTC ACCGGGGGT	49
10	(2)	INFORMAT	ION FOR SEQ ID NO:127:	
		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 54 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
15		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:127:	
	CAGT CGGT	CACGCT GC	IGGGTGGC CCTTACTCCC ACCGTGGCGG YGYCTTATAT	50 54
	(2)	INFORMAT	ION FOR SEQ ID NO:128:	
20		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 31 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:128:	
25	TAGC	ACTCTG GT	RGAYCTAC TCRCTGGAGG G	31
	(2)	INFORMAT	ION FOR SEQ ID NO:129:	
30		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 54 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:129:	
35	AAGT GAAT		GGGTGTC TCTCACCCCC ACCGTGGCTG CGCAACATCT	50 54

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0	(2)	INFORMATION FOR SEQ ID NO:130:										
		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 31 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear									
5		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:130:									
	AGGC	GCCATG GTC	GACCTGC TTGCAGGCGG C	31								
	(2)	INFORMATI	ON FOR SEQ ID NO:131:									
10		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 43 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear									
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:131:									
15	TCAG	CCCCGA VYY	TCGGAGC GGTCACGGCT CCTCTTCGGA GGG	43								
	(2)	INFORMATI	ON FOR SEQ ID NO:132:									
20		(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 44 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear									
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:132:									
	TGYT	ACGGAT YCC	CCARGTG GTCATHGACA TCATWGCCGG GGSC	44								
25	(2)	INFORMATI	ON FOR SEQ ID NO:133:									
30	·	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 40 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear									
		(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:133:									
	CATA	CCAAAT GCT	TCCACGC CCGCAACGGG ATTCCGCAGG	40								
35	(2)	INFORMATI	ON FOR SEQ ID NO:134:									

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J		(i	)		(B) (C)	LEN TYP STR	GTH:	37 nucl DNES	base eic	pai acid sing	rs				
		(x	i)		SEQU	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	134:		
5	TCT	TCTT	GCG	GGCG	CCGC	AG T	GGTT	TGCT	C AT	CCCT	G				37
	(2)	IN	FORM	ATIO:	N FO	R SE	Q ID	NO:	135:						
10		(i	)		SEQU (A) (B) (C) (D)	LEN TYP STR	GTH: E: ANDE	52 nucl DNES	base eic a S: a	pai: acid sing:	rs				
		(x	i)		SEQU	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	135:		
15	ATC' GC	TAGC.	ATC '	TTGA	GGGT	ac c	TGAG	ATTT(	G TG(	CGAG'	rgtg	ATA'	TTTG	GTG	50 52
	(2)	IN	FORM	ATIO	N FO	R SE	Q ID	NO:	136:						
20		(i	)		SEQUI (A) (B) (C) (D)	LENO TYP: STR	GTH: E: 8 ANDE	33 amino ONES	amino o aci S: u	o ac: id inkno	ids				
		(x	i)	8	SEQUI	ENCE	DES	CRIP'	rion:	: SEQ	) ID	NO:	136:		
	Trp	Ile	Gln	Val	Thr 5	Pro	Asn	Val	Ala	Val	Lys	His	Arg	Gly	Ala 15
25	Leu	Thr	His	Asn	_	Arg	Xaa	His	Xaa		Xaa	Ile	Val	Met	
	Ala	Thr	Val												
	(2)	IN	FORM	ATIOI	N FOI	R SE	Q ID	NO:	L37:						
30		(i)	)		SEQUI (A) (B) (C) (D)	TYPI STR	CHAIGTH: E: 6 ANDEI OLOGY	33 a amino ONESS	amino aci	aci id inkno	lds				
		(x:	i)	5	SEQUI	ENCE	DESC	CRIPT	rion:	SEC	] ID	NO:	L37:		
35	Trp	Val	Pro	Val	Ala 5	Pro	Asn	Leu	Ala	Ile 10	Ser	Gln	Pro	Gly	Ala 15

- 128 -Leu Thr Lys Gly Leu Arg Ala His Ile Asp Ile Ile Val Met Ser 20 25 Ala Thr Val INFORMATION FOR SEQ ID NO:138: (2) (1)SEQUENCE CHARACTERISTICS: 5 LENGTH: 33 amino acids (A) (B) TYPE: amino acid (C) STRANDEDNESS: unknown (D) TOPOLOGY: unknown (xi) SEQUENCE DESCRIPTION: SEQ ID NO:138: 10 Trp Ile Pro Val Xaa Pro Asn Val Ala Val Xaa Xaa Pro Gly Ala 10 Leu Thr Gln Gly Leu Arg Thr His Ile Asp Met Val Wal Met Ser Ala Thr Leu (2) INFORMATION FOR SEQ ID NO:139: 15 SEQUENCE CHARACTERISTICS: (i) (A) LENGTH: 33 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: unknown (D) TOPOLOGY: unknown 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:139: Trp Thr Xaa Val Thr Pro Thr Val Ala Val Arg Tyr Val Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val Gly Ala 20 Ala Thr Xaa (2) INFORMATION FOR SEQ ID NO:140:

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- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 33 amino acids
  - (B) TYPE: amino acid
  - STRANDEDNESS: unknown (C)
  - (D) TOPOLOGY: unknown
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:

Trp Val Ala Leu Xaa Pro Thr Leu Ala Ala Arg Asn Xaa Xaa Xaa Xaa Thr Xaa Xaa Ile Arg Xaa His Val Asp Leu Leu Val Gly Ala 20 25 35 Ala Xaa Phe

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(i)

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٥ (2) INFORMATION FOR SEQ ID NO:141: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 33 amino acids TYPE: amino acid STRANDEDNESS: unknown (C) TOPOLOGY: unknown (D) 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:141: Trp Val Xaa Xaa Xaa Pro Thr Val Ala Thr Arg Asp Gly Lys Leu 10 Pro Xaa Xaa Gln Leu Arg Arg Xaa Ile Asp Leu Leu Val Gly Ser 20 10 Ala Thr Leu INFORMATION FOR SEQ ID NO:142: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 33 amino acids TYPE: amino acid (B) (C) STRANDEDNESS: unknown 15 TOPOLOGY: unknown (xi) SEQUENCE DESCRIPTION: SEQ ID NO:142: Trp Thr Pro Val Thr Pro Thr Val Ala Val Ala His Pro Gly Ala Pro Leu Glu Ser Phe Arg Arg His Val Asp Leu Met Val Gly Ala 20 Ala Thr Leu INFORMATION FOR SEQ ID NO:143: (2) (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 33 amino acids 25 (B) TYPE: amino acid (C) STRANDEDNESS: unknown TOPOLOGY: unknown (D) (xi) SEQUENCE DESCRIPTION: SEQ ID NO:143: Trp Val Ala Leu Thr Pro Thr Val Ala Xaa Xaa Tyr Ile Gly Ala 30 Pro Leu Xaa Ser Xaa Arg Arg His Val Asp Leu Met Val Gly Ala 25 Ala Thr Val INFORMATION FOR SEQ ID NO:144: (2) 35

SEQUENCE CHARACTERISTICS:

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					(A) (B) (C) (D)	TYP	E: 8	amino ONES:	amino o ac: S: u unkno	id unkne					
		(x:	i)	:	SEQUI	BNCE	DES	CRIP'	TION	: SE	Q ID	NO:	144:		
5	Trp	Val	Ser	Leu	Thr	Pro	Thr	Val	Ala	Ala 10	Gln	His	Leu	Asn	Ala 15
	Pro	Leu	Glu	Ser	Leu 20	Arg	Arg	His	Val		Leu	Met	Val	Gly	
	Ala	Thr	Leu		20					23					70
10	(2)	IN	FORM	ATIO	N FOI	R SE	O ID	NO:	145:					*	
10		(i	)		SEQUI (A) (B) (C) (D)	LENG TYPI STR	E: 6 ANDEI	33 amino ONES	amino	o ac: id inkno	ids				
15		(x:	i)	9	SEQUI	BNCE	DES	CRIP:	rion:	: SE(	Q ID	NO:	L45:		
	Trp	Val	Pro	Leu	Thr 5	Pro	Thr	Val	Ala	Ala 10	Pro	Tyr	Pro	Asn	Ala 15
	Pro	Leu	Glu	Ser	_	Arg	Arg	His	Val		Leu	Met	Val	Gly	
	Ala	Thr	Met		20					23					30
20	(2)	IN	FORM	ATIO	N FOI	R SEQ	Q ID	NO:	146:						
25		(i	)		SEQUI (A) (B) (C) (D)	LENC TYPE STRA	STH: S: & ANDEI	33 amino ONESS	amino o aci	aci id inkno	ids				
23		(x:	i)		SEQUI	ENCE	DESC	CRIP	rion:	: SE(	) ID	NO:	L46:		
	Trp	Val	Xaa	Ile	Thr	Pro	Thr	Leu	Ser	_	Pro	Xaa	Xaa	Gly	
	Val	Thr	Ala	Pro	5 Leu	Arg	Arg	Xaa	Val	10 Asp	Tyr	Leu	Ala	Gly	
30	Ala	Ala	Leu		20					25					30
	(2)	IN	FORM	ATIOI	N FOI	SE(	O ID	NO:	L <b>4</b> 7:						
35		(i	)	•	SEQUI (A) (B) (C)	LENC TYPE STRE	TH: E: a ANDEI	33 a umino ONESS	amino o aci	aci ld inkno	ids				

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:147: Trp His Ala Val Thr Pro Thr Leu Ala Ile Pro Asn Ala Ser Thr 10 Pro Ala Thr Gly Phe Arg Arg His Val Asp Leu Leu Ala Gly Ala 25 Ala Val Val 5 (2) INFORMATION FOR SEQ ID NO:148: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 amino acids TYPE: amino acid (C) STRANDEDNESS: unknown 10 (D) TOPOLOGY: unknown (xi) SEQUENCE DESCRIPTION: SEQ ID NO:148: Thr Leu Thr Met Ile Leu Ala Tyr Ala Ala Arg Val Pro Glu Leu 10 15 Xaa Leu Xaa Val Val Phe Gly Gly 15 (2) INFORMATION FOR SEQ ID NO:149: SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 amino acids (B) TYPE: amino acid 20 (C) STRANDEDNESS: unknown (D) TOPOLOGY: unknown SEQUENCE DESCRIPTION: SEQ ID NO:149: (xi) Thr Thr Thr Met Leu Leu Ala Tyr Leu Val Arg Ile Pro Glu Val Ile Leu Asp Ile Val Thr Gly Gly 25 INFORMATION FOR SEQ ID NO:150: (2) SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: unknown 30 TOPOLOGY: unknown (D) SEQUENCE DESCRIPTION: SEQ ID NO:150: (xi) Thr Xaa Thr Xaa Ile Leu Ala Tyr Xaa Met Arg Val Pro Glu Val Ile Xaa Asp Ile Xaa Xaa Gly Ala 35

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_	(2)	(2) INFORMATION FOR SEQ ID NO:151:															
		(i)	)		(A) (B)	TYP:	ENCE CHARACTERISTICS: LENGTH: 23 amino acids TYPE: amino acid STRANDEDNESS: unknown TOPOLOGY: unknown										
5		( <b>x</b> ;	i)	8	SEQUI	ENCE	DES	CRIP'	rion:	SE	Q ID	NO:	151:				
	Ala	Val	Gly	Met	Val 5	Val	Ala	His	Xaa	Leu 10	Arg	Leu	Pro	Gln	Thr		
	Xaa	Phe	Asp	Ile	_	Ala	Gly	Ala									
10	(2)	IN	FORM	ATIO	N FO	R SE	Q ID	NO:	152:								
15		(i)	)		SEQUI (A) (B) (C) (D)	LENG TYPI STR	STH: E: & ANDEI	23 amino	amino aci	aci ld inkno	ids						
		( <b>x</b> :	i)	\$	SEQUI	ENCE	DES	CRIP'	rion :	SEÇ	Q ID	NO:	L52:				
	Thr	Xaa	Ala	Leu	Val	Xaa	Ser	Gln	Leu	Leu 10	Arg	Xaa	Pro	Gln	Ala 15		
20	Xaa	Xaa	Asp	Xaa	_	Xaa	Gly	Ala		10							
20	(2)	IN	FORM	ATIO	N FOI	R SE	O ID	NO:	L53:								
25		(i)	<b>)</b> ·		SEQUI (A) (B) (C) (D)	LENG TYPI STR	STH: E: 6 ANDEI	23 a amino ONES	amino aci	aci .d .nkno	ids						
		(x:	i)	5	SEQUI	ENCE	DESC	CRIP	CION:	SEC	OID	NO:	L53:				
	Thr	Xaa	Ala	Leu	Val 5	Xaa	Ala	Gln	Leu	Leu 10	Arg	Xaa	Pro	Gln	Ala 15		
30	Xaa	Leu	Asp	Met		Ala	Gly	Ala									
	(2)	IN	FORM	ATIOI	N FOI	R SE(	Q ID	<b>NO:</b>	L54:								
		(i)	)		SEQUI	LEN	ETH:	<b>2</b> 3 a	mino	aci							
35					(B) (C)	TYPE STR	ANDEI		aci 3: u	.d inkno	own						

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0 (D) TOPOLOGY: unknown (xi) SEQUENCE DESCRIPTION: SEQ ID NO:154: Thr Thr Leu Leu Leu Ala Gln Ile Met Arg Val Pro Thr Ala Phe Leu Asp Met Val Ala Gly Gly 20 5 (2) INFORMATION FOR SEQ ID NO:155: SEQUENCE CHARACTERISTICS: (i)(A) LENGTH: 23 amino acids (B) TYPE: amino acid 10 (C) STRANDEDNESS: unknown (D) TOPOLOGY: unknown (xi) SEQUENCE DESCRIPTION: SEQ ID NO:155: Thr Thr Thr Leu Xaa Leu Ala Gln Val Met Arg Ile Pro Ser Thr Leu Val Asp Leu Leu Xaa Gly Gly 15 20 (2) INFORMATION FOR SEQ ID NO:156: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 amino acids (B) TYPE: amino acid 20 (C) STRANDEDNESS: unknown (D) TOPOLOGY: unknown (xi) SEQUENCE DESCRIPTION: SEQ ID NO:156: Thr Ala Thr Leu Val Leu Ala Gln Leu Met Arg Ile Pro Gly Ala Met Val Asp Leu Leu Ala Gly Gly 25 20 (2) INFORMATION FOR SEQ ID NO:157: (i)SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 amino acids 30 (B) TYPE: amino acid (C) STRANDEDNESS: unknown TOPOLOGY: unknown (D) SEQUENCE DESCRIPTION: SEQ ID NO:157: (xi) Thr Ser Ala Leu Ile Met Ala Gln Ile Leu Arg Ile Pro Ser Ile 10 35

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0	Leu	Gly	Asp	Leu	Leu 20	Thr	Gly	Gly							
	(2)	IN	FORM	ATIO	N FOI	SE(	Q ID	NO:	158:						
5	, .	(i)				SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 amino acids  (B) TYPE: amino acid  (C) STRANDEDNESS: unknown  (D) TOPOLOGY: unknown									
		(x:	i)	5	SEQUI	ENCE	DESC	CRIP	rion:	: SE(	O ID	NO:	158:		
10	Xaa	Thr	Ala	Leu	Xaa 5	Met	Ala	Gln	Xaa	Leu 10	Arg	Ile	Pro	Gln	Va]
	Val	Ile	Asp	Ile	Ile 20	Ala	Gly	Xaa							
	(2)	IN	FORM	ATIOI	V FOI	SE(	QID	NO:	159:						
15		(i)	)		(A) (B) (C)	LENG TYPI STRI	STH: S: & ANDEI	23 amino	ERIST amino o aci S: u unkno	aci id inkno	ids				
		( <b>x</b> :	i)	5	SEQUI	ENCE	DESC	CRIPT	rion:	SEÇ	O ID	NO:	L59:		
20	Thr	Thr	Thr	Leu	Val	Leu	Ser	Ser	Ile	Leu 10	Arg	Val	Pro	Glu	Ile 15
	Cys	Ala	Ser	Val	Ile 20	Phe	Gly	Gly							

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#### CLAIMS

1. A cDNA of the envelope 1 gene of the hepatitis C virus wherein the cDNA has a sequence selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:51.

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2. A recombinant hepatitis C virus envelope 1 protein encoded by a gene whose sequence includes a sequence selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:51.

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- 3. A recombinant protein having an amino acid sequence selected from the group consisting of SEQ ID NO:52 through SEQ ID NO:102.
- 4. A method for the recombinant DNA-directed synthesis of at least one complete envelope 1 protein of hepatitis C virus said method comprising:

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culturing a transformed or transfected host organism containing a DNA sequence capable of directing the host organism to produce an envelope 1 protein under conditions such that the protein is produced, said protein exhibiting substantial homology to a protein comprising the amino acid sequence selected from the group consisting of SEQ ID NO:52 through SEQ ID NO:102.

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- 5. The method of claim 4, wherein the host organism is transfected with a recombinant eukaryotic expression vector.
  - 6. The method of claim 4, wherein the eukaryotic vector is a baculovirus vector.
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7. The method of claim 4, wherein the host

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organism is a eukaryotic cell.

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- 8. The method of claim 7, wherein the eukaryotic cell is an insect cell.
- 9. A recombinant expression vector comprising a cDNA sequence selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:51.
- 10. A host organism transformed or transfected10 with a recombinant expression vector according to claim 9.
  - 11. A method of detecting antibodies to HCV in a biological sample suspected of containing said antibodies comprising:
    - (a) contacting the sample with at least one recombinant protein of claim 3 to form an immune complex with the antibodies; and
    - (b) detecting the presence of the immune complex.
  - 12. The method of claim 11 wherein the biological sample is selected from the group consisting of serum, saliva or lymphocytes or other mononuclear cells.
  - 13. The method of claim 11, wherein the recombinant envelope 1 protein is bound to a solid support.
- 14. The method of claim 11, wherein the immune 30 complex is detected using a labeled antibody.
  - 15. A hepatitis C virus hit comprising: at least one recombinant protein comprising an amino acid sequence selected from the group consisting of: SEQ ID NO:52 through SEQ ID NO:102.

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16. A pharmaceutical composition comprising at least one recombinant protein of claim 3 and a suitable excipient, diluent or carrier.

- 17. A method of preventing hepatitis C

  5 infection, comprising administering the pharmaceutical composition of claim 16 to a mammal in an effective amount to stimulate the production of protective antibody.
- 18. A vaccine for immunizing a mammal against
  10 hepatitis C infection, comprising at least one recombinant
  protein according to claim 3 in a pharmacologically
  acceptable carrier.
- 19. A method for detecting the presence of the
  15 hepatitis C virus via a reverse transcription-polymerase
  chain reaction process, wherein the primers are selected
  from the sequences shown in SEQ ID NO:103 through in SEQ ID
  NO:108.
- 20. Substantially isolated and purified primers, wherein said primers have nucleic acid sequences selected from the group consisting of SEQ ID NO:103 through SEQ ID NO:108.
- 21. A diagnostic kit for use in detecting the presence of hepatitis C virus, said kit comprising: primers having nucleic acid sequences selected from the group consisting of SEQ ID NO:103 through SEQ ID NO:108.
- 30 22. A method for determining the genotype of a hepatitis C virus, said method comprising:
  - (a) amplifying RNA via reverse transcription-polymerase chain reaction to produce amplification products;
  - (b) contacting said products with at least

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one genotype-specific oligonucleotide;

- (c) detecting complexes of said products which bind to said oligonucleotide(s).
- 5 23. The method of claim 22, wherein said amplification of step (a) uses primer having a sequence according to SEQ ID NO:103 through SEQ ID NO:108.
- 24. The method of claim 23, wherein said oligonucleotide of the step (b) is a nucleic acid sequence selected from the group consisting of SEQ ID NO:109 through SEQ ID NO:135.
- 25. Substantially isolated and purified
  15 oligonucleotides, wherein said oligonucleotides have
  16 nucleic acid sequences selected from the group consisting
  17 of SEQ ID NO:109 through SEQ ID NO:135.
- 26. A diagnostic kit for determining the
  20 genotype of a hepatitis C virus, said kit comprising
  primers selected from the group consisting of SEQ ID NO:103
  through SEQ ID NO:108 and hybridization probes selected
  from the group consisting of SEQ ID NO:109 through SEQ ID
  NO:135.
  - 27. A substantially purified and isolated peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:136 through SEQ ID NO:159.
- 30 28. A method of detecting antibodies specific for a single genotype of HCV, said method comprising:
  - (a) contacting a biological sample with at least one peptide of claim 27 to form an immune complex with the antibodies, and

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(b) detecting the presence of the immune complex.

- 29. The method of claim 28, wherein the biological sample is selected from the group consisting of serum, saliva or lymphocytes or other mononuclear cells.
  - 30. The method of claim 28, wherein said peptide is bound to a solid support.
- 10 31. The method of claim 28, wherein the immune complex is detected using a labelled antibody.
- 32. A kit for use in detecting hepatitis C virus antibodies, said kit comprising: at least one peptide

  15 selected from the group consisting of SEQ ID NO:136 through SEQ ID NO:159.
- 33. A pharmaceutical composition comprising at least one peptide of claim 27 and a suitable excipient,20 diluent or carrier.
  - 34. A method of preventing hepatitis C infection, comprising administering the pharmaceutical composition of claim 33 to a mammal in an effective amount to stimulate production of a protective antibody.
- 35. A vaccine for immunizing a mammal against hepatitis C infection, comprising at least one peptide according to claim 27 in a pharmaceutically acceptable carrier.

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# FIGURE 1A

SEO ID NO:		_	
5	S14	1	TACCAAGTGCGCAACTCCACGGGGCTTTACCATGTLACCAATGATTGCCCTAACTCGAGTA
1	DK7	1	TACCAAGTGCGCAACTCCACGGGGCTTTACCATGTCACCAATGATTGCCCTAACTCGAGTA
В	<b>US11</b>	1	TACCAAGTACGCAACTCCACGGGGCTTTACCATGTCACCAATGATTGCCCTAACTCGAGTA
4	DR4	1	CACCAAGTGCGCAACTCTACAGGGCTTTACCATGTCACCAATGATTGCCCTAATTCGAGTA
3	DR1	1	CACCAAGTGCGCAACTCTACAGGGCTTTACCATGTCACCAATGATTGCCCTAATTCGAGTA
2	DK9	1	TACCAAGTACGCAACTCCtCGGGCCTcTACCATGTCACCAATGATTGCCCTAACTCGAGTA
6	S18	1	TACCAAGTACGCAACTCCaCGGGCCTTTACCATGTCACCAATGACTGCCCTAACTCGAGCA
_			
7	SWl	1	TACCAAGTACGCAACTCCtCGGGCCTTTACCATGTCACCAATGAtTGCCCTAACTCGAGtA
1-8	consensus		tACCAAGT-CGCAACTCcaCgGGGCTtTACCATGTcACCAATGAtTGCCCTAAcTCGAGtA
SEO ID NO:	Isolate		
5	S14	62	TEGTGTACGAGACAGCEGATGCEATCCTACACGCTCCGGGATGTGTCCCTTGCGTTCGEGA
1	DK7	62	Tegretaceaeecegeceateccatectecaeactcceeeegeretetcccreeeera
8	US11	62	TTGTGTACGAGGCGGCCGATGCCATCCTGCACACTCCGGGGTGTGTCCCTGCGTTCGCGA
4	DR4	62	TTGTGTACGAGGCGGCCGATGCCATCCTGCACACGCCGGGGTGTGTCCCTTGCGTTCGCGA
3	DR1	62	TTGTGTACGAGGCGGCCGATGCCATCCTGCACgCGCCGGGTGTGTCCCTTGCGTTCGCGA
2	DK9		TTGTGTACGAGGCGGCCGATGCCATCCTGCALTCTCCAGGGTGTGTCCCTTGCGTTCGCGA
6	\$18	62	TTGTGTACGAGACGGCCGATACCATCCTACACTCTCCgGGGTGTGTCCCTTGCGTTCGCGA
7	SW1	62	TTGTGTÀCGÀGÀCGGCCGATgCCATECTÀCACTCTCCaGGGTGTGTCCCCTTGCGTTCGCGÀ
1-8	consensus		TEGTGTACGAGGCGGCCGATGCCATCCTGCAC-CECCGGGGTGTGTCCCCTTGCGTTCGcGA
CEO TO NO.	T1		
SEO ID NO:	<u>Isolate</u> S14	123	GGGTAACacCTCGAGGTGTTGGGTGGCGATGACCCCCACGGTGGCCACCAGGGAcGGCAAA
1	DK7	123	GGGTAACGECTCGAGGTGTGGGTGGCGATGACCCCCACGGTGGCCACCAGGGAEGGCAAA
8	US11	123	GGGTAACGCtTCGAGGTGTTGGGTGGCGATGACCCCCACGGTGGCCACCAGGGACGGCAAA
4	DR4		GGGTACCCCCGAGGTGTTGGGTGGCGGTGACCCCCACGGTGGCCACCACGGAAA
_	-		
3	DR1	123	GGGTAACGCCTCGAGGTGTGGGTGGCCGGTGACCCCCACGGTGGCCACCAGGGACGGCAAA
2	DK9	123	ĠĠĠŦĂĂĊĠĊĊŦĊĠĂæAŦĠŦŦĠĠĠŦĠĠĊĠĠŦĠĠĊĊĊĊĂĊĠĠŦĠĠĊĀĊĠĠĠĂĀġ 
6	S18	123	GGGTAACGCCTCGAgATGTTGGGTGCCGGTGGCCCCCACAGTEGCCACCAGGGACGGCAAA
7	SW1	23	GGaTggCGCCcCGAagTGTTGGGTGgCGGTGGCCCCCACAGTcGCCACtAGGGACGGCAAA
1-8	consensus		GGgTaaCgcctCGAggTGTTGGGTGgCGgTGaCCCCCACgGTgGCCACcAGGGAcGGCAAa

# FIGURE 1A

SEO ID NO:	<u>Isolate</u>		
5	S14	184 CTCCCCgCAàCGCAGCTTCGACGTLACATCGATCTGCTLGTCGGGAGGGCCACCCTCTGT	T
1	DK7	184 CTCCCCACAGCGCAGCTTCGACGTCACATCGATCTGCTCGGGGAGGGCCCCCTCTGT	Ť
8	US11	184 CTCCCACAACGCAACTTCGACGTCACATCGATCTGCTTGTCGGGAGCGCCACCCTCTGT	Ť !
. 4	DR4	184 CHCCCACAACGCAGCTCGACGTCACATCGACCTGCTTGTCGGGAGCGCACCCTCTGC	T
3 .	DR1	184 CICCCACAACGCAGCITCGACGTCACATCGACCTGCTTGTCGGGAGCGCCACCCTCTGC	Ť
2	DK9	184 CTCCCGCAACGCTCGACGTCACATCGATCTGCTTGTCGGGAGCGCCACCCTCTGC	Ť
6	<b>S18</b>	184 CTCCCCGCAACGCAGCTTCGACGTCACATCGATCTGCTTGTEGGGAGCGCCACCCTCTGC	ľ
7	SW1	184 CTCCCtGCAACGCAGCTTCGACGTCACATCGATCTGCTTGTcGGaAGCGCCACCCTCTGC	r
1-8	consensus	CTCCCc-CA2CGCAGCTtCGACGTtACATCGAtCTGCTtGTtGGGGAGcGCCACCCTCTGc	Т
SEO ID NO:	<u>Isolate</u> S14	245 CGGCCCTCTACGTGGGGGACLTGTGCGGGTCTGTCTTCTTGTCGGTCAGCTGTTTACCT	ŗ
1	DK7	245 CGGCCCTCTACGTGGGGGACCTGTGCGGGTCTGTCTTTCTT	Т
8	S11	245 CGGCCTCTACGTGGGGGACCTGTGCGGGTCTGTCTTTCTT	ŗ
4	DR4		
3	DR1	245 CGGCCCTCTACGTGGGGGACCTGTGCGGGTCTGTCTTCCTTGTCGGTCAACTGTTCACCT	
2	DK9		ŗ
6	S18		ļ
7	SW1	245 CGGCCCTCTACGTGGGGGACLTGTGCGGGTCTGTCTTCTCGTCAGCCAACTGTTCACGT	r
1-8	consensus	CGGCCCTCTAcGTGGGGGAC-TGTGCGGGTCTGTCTTtCTtGTCgGtCAaCTGTTcACct	
		-	
SEO ID NO:	<u>Isolate</u> S14	306 CTCTCCCAGGCGCCLCTGGACGACGCAAGACTGCAATTGTTCTATCTATCCCGGCCATAT	A
1	DK7		1
8	S11		A
4	DR4	306 CTCCCAGGCACTGGACAACGCAAGACTGCAATTGTTCCATCTATCCCGGCCATATA	Į A
3	DR1	306 ETCTCCCAGGCGCACTGGACAGCGCAAGACTGCAATTGTTCTATCTA	1
_	DK1		
2			
. 6	S18	306 CTCCCCAGGCGCCACTGGACAACGCAAGACTGCAACTGTTCTATCTA	1
7	SW1	306 CTCCCCAGGCGCACTGGACAACGCAAGACTGLAACTGTTCTATCTALCCCGGCCACAT	
_ 1-8	consensus	cTCtCCAGgCgCCaCTGGACaACGCAaGaCTGcAAtTGTTCtATCTAtCCcGGCCAtATa	1

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# FIGURE 1A

SEO ID NO:	Isolate	2 CT
5	S14	367 ACGGGTCL:CGCATGGCaTGGGATATGATGAACTGGTCCCCTACgACGGCacTGGTAG
1	DK7	367 ÁCGGGTCÁCCGCÁTGGCgTGGGÁTÁTGÁTGÁTGÁACTGGTCCCCTÁCCÁCGGCGTTGGTÁG
8	S11	367 ACGGGTCACCGCATGGCATGGGATATGATGATGACTGGTCCCCTACGGCGGCGTTGGTGG
4	DR4	367 ACGGGCCACCGCATGGCGTGGGATATGATGATGACTGGTCCCCTACGACAGCGCTGGTAG
3	DR1	367 ACGGGACACCGEATGGCATGGGATATGATGAACTGGTCCCCTACGACAGCGCTGGTAA
2	DK9	367 ACGGGTCALCGCATGGCgTGGGATATGATGATGAACTGGTCCCCTACAGCAGCGCTGGTAA
6	S18	367 ACGGGTCACCGLATGGCATGGGATATGATGAACTGGTCCCCTACAACGGCGLTGGTAA
7	SW1	
1-8		ACGGGtCAcCGcATGGCaTGGGATATGATGATGACTGGTCCCCtACGaC-GCGCTGGTATGATGTAGTAGTAGTAGTAGTAGTAGTAGTAGTAG
1-0	consensus	ACGGCCACCGCATGGCATGGATATGATGATCGGTCGCCCCACGGCTGGTAG
SEO ID NO:	Isolate	
5	S14	428 TAGCTCAGCTGCTCCGGATCCCaCAAGCCATCTTGGAtATGATCGCTGGTGCTCACTGGGG
1	DK7	428 TÁGCTCÁGCTGCTCCGGATCCCGCAAGCCATCTTGGACATGATCGCTGGTGCTCACTGGGG
8	S11	1
4	DR4	428 TAGCTCAGCTGCTCCGGATCCCACAAGCCATCTTGGACATGATCGCTGGTGCCCACTGGGG
3	DR1	428 TGGCTCAGCTGCTCCGGATCCCACAAGCCATCTTGGACATGATCGCTGGAGCCCACTGGGG
_		
2	DK9	428 ŤĠĠĊġĊĂĠĊŤĠĊŤĊĀĠĠĂŤĊĊĊĠĊĀġĠĊĊĀŤĊĬŤĠĠĀĊĀŤĠĀŤĊĠĊŢĠĊŢĠĊĊĊĀĊŢĠĠĠ 
6	S18	428 ŤAĠĊŤĊÁĠĊŤĠĊŤĊÁĠĠġŤĊĊĊĠĊĂĀĠĊĊĠŤĊĬŤĠĠĂĊÁŤĠĂŤĊĠĊŤĠĊŤĠĊĊĊĀĊŤĠĠĠĠ
7	SW1	428 TAGCTCAGCTCAGGATCCCGCAAGCCGTCTTGGACATGATCGCTGGTGCCCACTGGGG
1-8	consensus	TagCtCAGCTGCTCcGGaTCCC-CAagCCaTCTTGGAcATGATCGCTGGtGCcCACTGGGG
SEO ID NO:	<u>Isolate</u> S14	489 AGTCCTAGCGGGCATAGCGTATTTCTCCATGGTGGGAAACTGGGCGAAGGTCCTAGTgGTG
_		
1	DK7	489 AGTCCTgGCGGGCATAGCGTATTTLTCCATGGTGGGGAACTGGGCGAAGGTCCTGGTAGTG
8	S11	489 ÁĞTCTAĞCĞĞCĞTAĞTĞTATTTCTCCATĞĞTĞĞĞĞAACTĞĞĞCĞAAĞĞTCCTĞĞTAĞTĞ
4	DR4	489 AGTCCTAGCGGCATAGCGTATTCTCCATGGTGGGGAACTGGGCGAAGGTCCTGGTAGTG
3	DR1	489 AGTCCTAGCGGCATAGCGTATTTCTCCATGGTGGGAACTGGGCGAAGGTCGTGGTAGTG
2	DK9	489 AGTCCTAGCGGGCATAGCGTATTTCTCCATGGTGGGGAACTGGGCGAAGGTCGTGGTGGTA
6	S18	489 AGTCCTAGCGGGCATAGCGTATTTCTCCATGGGGGGAACTGGGCGAAGGTCCTGCTAGTG
7	SW1	489 AGTCCTAGCGGGCATAGCGTATTTCTCCATGGtGGGGAACTGGGCGAAGGTCCTGATAGTG
1-8	consensus	AGTCCTAGCGGGCATAGCGTATTTcTCCATGGtGGGGAACTGGGCGAAGGTCcTggTaGTg

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## FIGURE 1A

Isolate		
S14	550	CTGCTGCTATTCGCCGGCGTtGACGCG
nr7	550	CTGCTGCTATTTGCCGGCGTCGACGCG
DK,	250	
US11	550	CIGCIGCIATTIGCCGCCGTCGACGCG
DR4	550	CIGITGCIGITIGCCGGCGTTGATGCG
		1111111111111111111111111111
ומת	550	CIGITGCIGITTGCCGGCGTTGATGCG
DRI	230	
DK9	550	CTGTTGCTGTTTaCCGGCGTCGATGCG
\$1.8	550	CIGITGCIGITT9CCGGCGTCGATGCG
220		
SWI	550	CTGTTGCTGTTTtCCGGCGTCGATGCG
consensus		CTGtTGCTgTTtgCCGGCGTcGAtGCG
	DK7 US11 DR4 DR1	S14 550 DK7 550 US11 550 DR4 550 DR1 550 DK9 550 S18 550 SW1 550

SEO ID NO:	<u>Isolate</u>	
11	DK1	1 TATGAAGTGCGCAACGTGTCCGGGGTGTACCACGTCACaAACGACTGCTCCAACTCAAGCA
. 24	TlO	
7 42		
10	D3	1 TATGAAGTGCGCAACGTGTCCGGGGTGTACCAAGTCACCAAtGACTGTTCCAACTCGAGCA
• 9	<b>D1</b>	1 TATGAAGTGCGCAACGTGTCCGGGGTGTACCATGTCACGAACGA
•		
14	HKS	1 TATGAAGTGOGCAACGTGTCCGGGGTATACCATGTCACGAACGACTGCTCCAACTLAAGCA
15	HK8	1 TATGAAGTGCGCAACGTGTCCGGGATATACCATGTCACGAACGA
12	HK3	1 TATGAAGTGCGCAACGTGTCCGGGATATACCATGTCACGAACGA
23	Т3	1 TACGAAGTGCGCAACGTGTCCGGGGTGTACLATGTCACGAACGACTGTTCCAACTCAAGCA
22	SW2	1 TATGAAGTGCGCAACGTGTCCGGGGTGTALCATGTCACGAACGACTGTTCCAACTCAAGCA
17	IND8	1 TATGAGTGCGCAACGTGTCCGGGGTGTACCATGTCACGAACGA
17	INDO	
16	IND5	1 TATGAAGTGCGCAACGTGTCCGGGGTGTACCATGTCACGAACGA
21	SA10	1 TATGAAGTGCGCAACGTGTCCGGGATGTACCATGTCACGAACGA
	anz v	
20	S45	1 TATGAAGTGCGCAACGTGTCCGGGGCGTACCATGTCACGAACGA
25	US6	1 TATGAAGTGCGCAACGTGTCCGGGATGTACCATGTCACGAACGA
	050	
13	HK4	1 CATGAAGTGCaCAACGTaTCCGGGATCTACCATGTCACGAACGACTGCTCCAACTCAAGTA
18	P10	1 TATGAAGTGCGCAACGTGTCCGGGGTGTACCATGTCACGAACGA
19	S9	1 TATGAAGTGCGCAACGTaTCCGGGGCGTACCATGTCACGAACGACTGCTCCAACTCAAGTA
9-25	consensus	tatgaagtgcgcaacgtgtccggggtgtaccatgtcacgaacga

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SEO ID NO:	<u> Isolate</u>		
11	DK1	62	TeGTGTaTGAGGCAGtGGACGTGATCATGCAtACCCCaGGGTGCGTGCCCTGCGTTCGGGA
24	T10	62	TEGTGTETGAGGCAGCGGACETGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCGGGA
4			Trementa Teagrage Carrier Transport Andrews Court Cour
10	D3	62	TCGTGTATGAGACAGCGGACATGATCATGCACACCCCCGGGTGCCTTGCGTTCGGGA
_			
, 9	Dl	64	TEGTGTATGAGACAGCGGACATGATCATGCACACCCCCGGGTGCGTGC
4.4	HK5	62	TCGTGTACGAGACARCGGACATGATCATGCACACCCCTGGGTGCCCTGCGTTCGGGA
14	AA.	02	
15	HK8	62	TOTTETATGAACAGCGGACATGATLATGCATACCCCTGGGATGCATGCCCTGCGTTCGGGA
23	2210	-	
12	HK3	62	TCGTGTATGAGACAGCaGACATGATCATGCATACCCCTGGATGCGTGCCCTGCGTaCGGGA
23	<b>T</b> 3	62	TTGTGTATGAGACAGCGGACATGATCATGCACACCCCTGGGTGCCCTGCGTTCGGGA
22	SW2	62	TIGTGTATGAGACAGCGGACATGATCATGCALACCCCCGGGTGCGTGCCCTGCGTTCGGGA
17	IND8	62	TIGIGTATGAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGC
16	IND5	62	TTGTGTATGAGGCAGCGGACATGATCATGCACACECCCGGGTGCGTGCCCTGCGTTCGGGA
21	SA10	62	TTGTGTATGAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGC
			TYCTYCTATGAGGCAGEGGACCTGATCCTGCACACCCCEGGGTGCCTGCCCTTGCGGA
20	S45	62	TTGTGTATGAGGCAGtGGACGTGATCcTGCACACCCCtGGGTGCGCCCTGCGTTCGGGA
25	<b>US</b> 6	62	TYSTCTATGACGCAGCGACATGATCATGCACACCCCGGGTGCGTGC
43	036	02	
13	HK4	62	TTGTGTATGAGGCAGCGGACATGATCATGCALACCCCCGGGTGCGTGCCCTGcGTcCGGGA
43	244.2	-	
18	P10	62	TTGTGTATGAGGCAGCGGACATGATaATGCACACCCCCGGGTGCGTGCCCTGtGTTCGGGA
19	<b>S9</b>	62	TIGIGIA-GAGGCAGCGGACGTGATCATGCALACCCCCGGGTGLGTACCCTGCGTTCAGGA
9-25	consensus		TtGTGTatGAggCAgcgGACaTGATcaTGCAcACcCCcGGgTGcgTgCCCTGcGTtCgGGA

SEO ID NO:	<u> Isolate</u>		
11	DKI	123	GAACAACCACTCCCGETGCTGGGTAGCGCTCACCCCCACGCTCGCGGGCCAGGAACGCCAGC
24	T10	123	GGGCAACTCCTCCCGCTGCTGGGTAGCGCTCACtCCCACGCTCGCGGCCAGGAACACCAGC
	<b>D</b> 3	177	GGACAACTCCTCTCGCTGCTGGGTAGCGCTCACCCCCCACGCTCGCGGCTAGGAATAGCAGC
10	נע	123	
9	D1	123	GGACAACTCCTCTCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCGGCTAGGAATGGCAAC
14	HK5	123	AACAACTCCTCCCGTTGETGGGTAGCGCTCGCCCCCACGCTCGCGGCCAGGAAcGcCAGC
15	HK8	123	GAACAACTCCTCCCGTTGCTGGGTgGCGCTCACTCCCACGCTCGCGGCLAGGAALGTCAGC
12	HK3	123	GAACAACTCCTCCCGCTGtTGGGTAGCGCTCACTCCCACGCTCGCGGCCAGGAACGTCAGC
23	T3	123	GAGCAALTCCTCCCGCTGCTGGGTAGCGCTLACTCCCACGCTCGCGGCCAGGAACGCCAGC
22	SW2	122	GGCCAACTCCTCCCGCTGCTGGGTAGCGCTCACTCCCACGCTaGCaGCCAGGAACACCAGC
44	3#2	123	11 1111 111 1 1111111111111111111111111
17	INDS	123	GGGCAACTECTCTaGETGCTGGGTAGCGCTCACTCCCACTCTCGCGGCLAGGAACGCCAGC
16	IND5	123	GGGCAACTCCTCTCGCTGGTAGCGCTCACTCCCACTCTCGCGGCCAGGAACGCCAGC
21	SALO	123	GAACAACTCCTCCCGCTGCTGGGTAGCGCTCACTCCCACGCTCGCGGCCAGGAACTCCAGC
			GAACACTCCTCCCGtTGCTGGGTGGCGCTCACTCCCACGCTCGCGGCCAGGAACTCCAGC
20	S45	123	GAACAACTCCTCCCGtTGCTGGGTGGCGCTCACTCCCACGCTCGCGGCCAGGAACTCCAGC
25	US6	123	GAACAA+TCCTCCGCTGCTGGGTAGCGCTCACTCCCACGCTCGCGGCCAGGAACGC+AGC
23	450		
13	HK4	123	GAACAACTCCTCCCGETGCTGGGTAGCGCTCACTCCCACGCTCGCGGCCAGGAACGCCAGC
18	P10	123	GAACAACTCCTCCCGCTGCTGGGTAGCGCTCACTCCCACACTCGCGGCLAGGAALLCCAGC
19	S9	123	GggtAACTCCTCCCaaTGCTGGGTgGCGCTCACcCCCACgCTCGCGGCcAGGAAcgCtAcC
9-25	consensus		gaacAActcCTCccgcTGcTGGGTaGCGCTcaCtCCCACgCTcGCgGCcAGGAAcgccAgC

SEO ID NO:	<u>Isolate</u>		
11	DKI	184	atccccactacgacaatacgacgccatgtcgatttgctcgttggggcggctgctttctgct
24	T10	184	GTCCCCACTACGACGATACGACGCCATGTCGATTTGCTCGTTGGGGCGGCTGCTTTCTGCT
•			
10	D3	184	GTCCCCACTACGACaATACGACGCCACGTCGATTIGCTCGTTGGGGCGGCIGCTTTCTGCT
_			
, 9	D1	184	GTCCCCACTACGGCgATACGACGCCACGTCGATTTGCTCGTTGGGGCCGCTTTCTGCT
			GTCCCCACGCCATACGACGCCACGTCGACTTGCTCGTTGGGGCGGCTGCTTTCTGCT
14	HIG	184	GICCCACACACACACACACACACACACACACACACACACA
	••••	7.04	
15	HK8	184	IIIIIII IIIIIIIIIIIIIIIIIIIIIIIIIIIIII
4.7	HK3	184	CITCCCPACCACCACTACCACCTCACCTCGACTCGCTCGCTCGCCGGCGGCCGCCTCTCTGCT
12	AK-3	704	
23	Т3	184	GTCCCCACTARGACAATACGACGTCACGTCGACTTGCTCGTTGGGGCGGCTGCTTTCTGET
23		202	
22	SW2	184	GTCCCCACTACGACAATACGACGCCACGTCGATTTGCTCGTTGGGGCGGCTGCTTTCTGCT
44	J2		
17	IND8	184	GTCCCCACCACGACAATACGACGCCACGTCGATTTGCTCGTTGGGGCGGCTGCTTTCTGTT
• '			
16	INDS	184	GTCtCCACCACGACAATACGACACCACGTCGATTTGCTCGTTGGGGCGGCTGCTTTCTGTT
21	SA10	184	GTCCCCACTACGACAATACGACGCCACGTCGATTTGCTCGTTGGGGCGGCTGCTTTCTGCT
20	S45	184	GTCCCCACTACGACAATACGACGECACGTCGATTTGCTCGTTGGGGCGGCTGCTTTCTGCT
25	US6	184	GTCCCCACTACGACAATACGACGCCACGTCGATTTGCTCGTTGGGGCGGCTaCTTTCTGCT
13	HK4	184	atccccactacgacaatacgacgccatgtcgacttgctcgttgggggggg
18	P10	184	GTCCCaACTACGGCAATACGACGCCATGTCGATTTGCTCGTTGGGGCGGCGCTGCTTTCTGCT
			CTCCCACCACCACACATTCGACGCCATTTCGCTCGTTGGGGCGGCTGTTTCTGCT
19	S9	184	ĠŦĊĊĊcĂĊcĂĊĠaĊĂĂŦĂĊĠĂĊĠĿĊĂŦĠŦĊĠĂŦŦĠĊŦĊĠŦŦĠĠĠĠĠĠĠĠĊŦĠĿŦŦŦĊŦĠĊŦ
9-25	consensus		gtcccactacgacatacgacgccacgtcgattgctcgttggggcggctgctttctgct

SEO ID NO:	<u>Isolate</u>		
11	DK1	245	CCGCTATGTACGTGGGGGACCTCTGCGGATCCGTTTTCCTCGTCTCTCAGCTGTTCACCTT
24	TlO	245	CCGCTATGTALGTGGGAGACCTCTGCGGATCTGTTTTCCTCGTCTCTCAGCTGTTCACCTT
•			
10	<b>D</b> 3	245	COGCCATGTACGTGGGGGATCT-TGCGGATCTGTTTTCCTCGTCTCCCAGCTGTTCACCTT
. 9	D1	245	COSCCATGTACGTGGGGGATCTCTGCGGATCTGTTTTCCTCATCTCCCAGCTGTTCACCCT
14	HK5	245	COSCTATGTACGTGGGGGATCTTTGCGGATCTGTTTTCCTCGTCTCCCAGCTGTTCACCTT
15	HK8	245	CCGCTATGTACGTGGGGGATCTCTGCGGATCTGTTTTCCTCGTCTCCCAGCTGTTCACCTT
12	HK3	245	CCGCTATGTACGTGGGGGATCTCTGCGGATCTGTTTTCCTLGTCTCCCAGCTGTTCACCTT
23	<b>T</b> 3	245	CCGCTATGTACGTGGGGGATCTCTGCGGATCTGTTTTCCTCGTCTCCCAGCTGTTCACTTT
22	SW2	245	CCGLTATGTACGTGGGGGATCTCTGCGGATCTGTTTTCCTCGTCTCCCAGCTGTTCACTTT
17	IND8	245	CCGCTATGTACGTGGGGGATCTCTGCGGATCTGTTTTCCTLGTCTCCCAGCTGTTCACCTT
16	IND5	245	CCGCTATGTACGTGGGGGATCTATGCGGATCTGTTTTCCTCGTCTCCCAGCTGTTCACCTT
21	SA10	245	CCGCcATGTACGTGGGGGA-CTCTGCGGATCTGTTTTCCTTGTCTCCCAGCTGTTCACCTT
20	<b>S4</b> 5	245	CCGCTATGTACGTGGGGGAECTCTGCGGATCTGTTTTCCTTGTETCCCAGCTGTTCACCTT
25	US6	245	CCGCTATGTACGTGGGGGACCTCTGCGGGTCCGTTTTCCTCATCTCCCAGCTGTTCACCTT
13	HK4	245	CCGCcATGTACGTGGGAGATCTCTGCGGATCTGTCTCCCAGCTGTTCACCTT
18	P10	245	CCGCTATGTACGTGGGGGATCTCTGCGGATCTGTTCTCCCAGCTGTTCACCTT
19	S9	245	CCGCTATGTACGTGGGGGACCTGTGCGGATCTGTTETCCTCATCTCCCAGCTGTTCACCAT
9-25	consensus		CCGctATGTAcGTGGGGGAtCTcTGCGGATCtGTttTCCTcgTcTCcCAGcTGTTCACctT

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SEO ID NO:	<u>Isolate</u>		
11	DK1	06 tTCaCCTCGCCGGC	ATGAGACagcaCAGGACTGCAACTGCTCAATCTATCCCGGCCAcgTt
24	TlO	06 CTCGCCTCGCCGGC	ATGAGACEET CAGGACTGCAACTGCTCAATCTATCCCGGCCAECTG
44	110		
10	<b>D</b> 3	os credecredecede	ATGAGACAGTACAGGAATGTAACTGCTCAATCTATCCCGGCCACGTG
_	81	06 CTCGCCTCGCCGGC	
9	D1	111111111111	
14	HKS	OF CTCGCCTCGCCGAC	accacación de la contra del la contra del la contra del la contra del la contra de la contra de la contra del la contra
15	HK8	06 trogcorogeogac	ACCAGALOGIALAGGALIGCAALIGCI CAAICIAICCCGGCCALGIA
12	HIG	06 CTCGCCTCGCCGAC	ACGAGACAGTACAGGACTGCAACTGCTCACTCTATCCCGGCCACGTA
			1
23	<b>T</b> 3	oe creeccreeceec	Atgagacagtacaggactgcaactgctcaatctatcccggccacgta
22	SW2	06 tTCACCTCGCCGGC	
22	3#2	11111 111111	
17	IND8	os creacedecede	ATGAGACAGTACAGGACTGCAATTGCTCCATCTATCCCGGCCACGTA
_		111111111111111111111111111111111111111	
16	IND5	06 CTCACCGCGCCGGC	ATGAGACAGTACAGGACTGCAATTGCTCCATCTATCCCGGCCACGTA
21	SA10	06 CTCGCCTCGCCGGt	atgagacagtacaggactgcaattgctcaatctatcccggccgcgta
20	S45	06 CTCGCCTCGTCGGC	ATGAGACAGTACAGGACTGCAACTGTTCAATCTATCCCGGCCACGTA
25	US6	06 CTCGCCTCGTCaGC	ATGAGACAGTACAGGACTGCAATTGTTCAATCTATCCCGGCCACGTA
45	000	11111111111	
13	HK4	os cicáccicaccasc	ATGAGAC 9GTACAGGACTGCAATTGCTCAATCTATCCCGGCCACGTA
=0	D1 0	06 GTC-CGTCGCCGGC	}
18	P10	06 CTCaCCTCGCCGGC	
19	S9	06 CICGCCCCGtCGGC	ArgaGACAGTACAGaACTGCAATTGCTCAATCTATCCCGGaCACGTg
9-25	consensus	cTCgCCtCGcCggc	AtgaGACagtaCAGgAcTGcAAcTGcTCaaTCTATCCcGGcCacgTa

SEO ID NO	: Isolate		
11	DK1.	367 TCAGGTCACCGCATGGCTTGGGALATGATGATGAACTGGTCACCTACAACAGCCCTAC	<b>JTG</b> C
			111
24	T10	367 TCAGGTCACCGCATGGCTTGGGACATGATGATGAACTGGTCGCCTACAACAGCECTAC	GTGG
			1111
10	<b>D</b> 3	367 ACAGGTCACCGCATGGCTTGGGATATGATGAACTGGTCGCCTACAGCAGCCCTAC	FIGG
9	Dl	367 ÁCÁGGTCÁCCGLATGGCTTGGGATATGATGATGACTGGTCACCTÁCÁACÁGCCLTÁC	<b>FIGG</b>
			1111
14	HK5	367 ACAGGTCACCGCATGGCTTGGGATATGATGATGACTGGTCACCTACAACAGCCCTAC	FIGG
			1111
15	HIK8	367 TÖÁGGTCACCGCATGGCTTGGGATATGATGATGACTGGTCGCCACÁCÁGCCCCTÁC	FIGG
			1111
12	HK3	367 TCAGGTCACCGCATGGCTTGGGATATGATGATGACTGGTCGCCLACAGCAGCCCTAC	STGG
			1111
23	<b>T</b> 3	367 aCAGGTCACCGLATGGCTTGGGATATGATGATGACTGGTCGCCCACAACGGCACTAC	FIGG
			1111
22	SW2	367 TCÁGGTCÁCCGCATGGCTTGGGACATGATGATGACTGGTCACCTACÁGCAGCCCTTG	STGG
17	IND8	367 ŤĊŘĠĠŤĊŘĊĊĠĊŔŤĠĠĊŤŤĠĠĠŘŤŘŤĠŘŤĠŘŤĠŘČŤĠĠŤĊŔĊĊŤŘĊŘĠĊġĠĊĊĊŤŔĊ	TGG
16	IND5	367 ŤĊÁĠĠŤĊÁĊĊĠĊÁŤĠĠĊĸŤĠĠĠĂŤÁŤĠĂŤĠÁŤĠÁĊŤĠĠŤĊÁĊĊŤÁĊÁĠĊAĠĊĊĊŤÁĊ	TGG
21	SA10	367 ACÁĞĞTCACCĞCATĞĞCTTĞĞĞATATĞATĞATĞAĞCTĞĞTCACCTACAACAĞCLCTAC	TaG
			11 1
20	S45	367 ÁCÁGGTCÁCCGCÁTGGCTTGGGÁTÁTGATGÁTGÁCTGGTCGCCTÁCÁGCÁGCCCTÁC	JTGG
25	US6	367 TCAGGTCACCGCATGGCTTGGGATATGATGATGAAtTGGTCACCTACAGCAGCCCTAC	TGG
13	HK4	367 TCAGGTCACCGCATGGCTTGGGATATGATGATGAACTGGTCACCTACAGCAGCCCTAC	FTGG
			111
18	P10	367 TCAGGTCACCGCATGGCTTGGGATATGATGATGAACTGGTCGCCCACAGCAGCCCCTAG	TGG
			111
19	S9	367 aCAGGTCALCGCATGGCCTGGGATATGATGAACTGGTCGCCLACAACAGCCCTAG	iTGG
9-25	consensus	tcaggtcaccgcatggcttgggalatgatgatgaactggtcacclacagcagccctag	Tgg

SEQ ID NO:	<b>Isolate</b>		
11	LK1	428	TaTCGCAGTTACTCCGaATCCCACAAGCTGTCgTGGACATGGTGgCgGGGCCCACTGGGG
24	<b>T10</b>	428	TGTCGCAGTTACTCCGGATCCCACAGCTGTCaTGGACATGGTGaCaGGGGCCCACTGGGG
10	<b>D</b> 3	428	TATCGCAGTTACTCCGGATCCCACAAGCTGTCgTGGACATGGTGGCGGGGGCCCACTGGGG
. 9	D1	428	TATCGCAGTTACTCCGGATCCCACAAGCTGTCaTGGACATGGTGGCGGGGGCCCACTGGGG
14	HK5	428	TGTCGCAGTTACTCCGGATCCCGCAAGCTGTCGTGGACATGGTAGCGGGGGCCCACTGGGG
15	HK8	428	TGTCGCAGTTACTCCGGATCCCGCAAGCTaTCGTGGACATGGTGGCGGGGCCCACTGGGG
12	HK3	428	TGTCGCAaTTACTCCGGATCCCGCAAGCTGTCGTGGACATGGTGGCGGGGGCCCACTGGGG
			TETCECAGTTCCTCCGGATCCCACAAGCTGTCGTGGACATGGTGGCGGGGCCCACTGGGG
23	<b>T</b> 3	428	TGTCGCAGTTGCTCCGCATCCCACAAGCTGTCGTGGACATGGTGGCGGGGCCCACTGGGG
22	SW2	428	TATEGRAFITAL TOUGATECTA AAGE ISTESSAA TIGSTAGE ISTESSAGE CALEGOS
17	IND8	428	TATOGCASTIGCICCOCATCCACAAGCIGICGIGGATATGGIGGIGGGGGCCCACIGGGG
16	IND5	428	TATUGCASTIGCTCCGGALCCCACAGGCIGCGIGGATALGGIGGCGGGGCCCACLGGGG
	SA10	428	THE CONTROL OF CONTROL OF THE CONTRO
21	SAIU	440	INTEGERGIACICCOCCICCACCICACCICCACCICCACCICCACCICACCICACCICCACCICACCICACCICACCICCACCIC
20	S45	428	TRITICAGETTACTCCGGATCCCACAGCTGTCGTGGACATGGTGGCGGGGGCCCACTGGGG
20	242	420	
25	บร6	428	TATCCCAGTTACTCCGGATCCCACAGCTGTCATGGACATGGTGGCGGGGCCCACTGGGG
	•		
13	HK4	428	TATCGCAGTTACTCCGacTCCCACAAGCTGTCATGGACATGGTGGCGGGAGCCCACTGGGG
18	P10	428	TGTCGCAGCTACTCCGGATCCCACAGCTaTCtTGGATGTGGTGGCGGGGCCCACTGGGG
19	S9	428	TaTCGCAGCTACTCCGGATCCCACAGCTGTCaTGGATaTGGTGGCGGGGCCCACTGGGG
_ <del>-</del>			
9-25	consensus		TaTCGCAgtTaCTCCGgaTCCCaCAAGCTgTCgTGGAcaTGGTggCgGGGGCCCACTGGGG

SEO ID NO:	<u>Isolate</u>		
11	DKI	9 AGTCCTEGCGGGCCTCGCCTACTAC	TCCATGGCGGGAACTGGGCCAAGGTTTTAATTGTG
•	T10	9 AGTCCTGGCGGGCCTEGCCTACTAT	
24	110		
. 10	D3	9 GGTCCTGGCGGGCCTCGCCTACTAT	TCCATGGTGGGGAACTGGGCTAAGGTTTTGATTGTG
. 9	D1	9 GGTCCTGGCGGGCCTCGCCTACTAT	TCCATGGTGGGGAACTGGGCTAAGGTTTTGATTGTG
14	HKS	111111111111111111111111111111111111111	111111111111111111111111111111111111111
15	HKS	9 AGTCCTAGCGGGCCTTGCCTACTAT	TCCATGGTGGGCAACTGGGCTAAGGTTTTGATTGTG
***			
12	HK3	9 AGTCCTAGCGGGCCTTGCCTACTAT	TCCATGGTGGGAAACTGGGCTAAGGTTTTGATTGTG
23	<b>T</b> 3	9 AGTCCTGGCGGGCCTTGCCTACTAT	TCCATGGTGGGGAACTGGGCTAAGGTTTTGATTGTG
	SW2	9 AGTCCTGGCGGGCCTTGCaTACTAT	TCCATGGTGGGGAACTGGGCTAAGGTTTTGATTGTG
22	5W2	AGICCIGGGGGGCCIIGCAIACIAI	1111111 1111111111111111111111111111111
17	IND8	9 AATCCTGGCGGGCCTTGCCTACTAT	TCCATGGTAGGGAACTGGGCTAAGGTTTTGATTGTG
	2.50		
16	IND5	9 AATCCTGGCGGGCCTTGCCTACTAT	TCCATGGTAGGGAACTGGGCTAAGGTTTTGATTGTG
		<u> </u>	
21	SA10	AGTCCTAGCGGGCCTTGCCTACTAT	TCCATGGTGGGGAACTGGGCTAAGGTTTTGATTGT
20	S45	9 AGTCCTGGCGGGCCTTGCCTACTAT	TCCATGGTGGGGAACTGGGCTAAGGTTCTGATTGTG
20	313		
25	US6	9 AGTCCTGGCGGGCCTTGCCTACTAT	TCCATGGTGGGGAACTGGGCTAAGGTTCTGATTGTG
13	HK4	9 AGTCCTAGCGGGCCTTGCtTACTAT	TCCATGGTGGGGAACTGGGCCAAGGTTTTGATTGTG
	710		TCCATGGTGGGGAACTGGGCTAAGGTCTTGATTGTG
18	P10	111111111111111111111111111111111111111	
19	S9	9 AGTCCTGGCGGGCCTCGCCTACTAT	TCCATGGTGGGGAACTGGGCTAAGGTLTTGATTGTG
9-25	consensus	agTCCTgGCGGGCCTtGCcTACTAt	TCCATGGtgGGAACTGGGCtAAGGTttTgATTGTg

	_ •		
SEO ID NO:	<u>Isolate</u> DK1	EEA	tTGCTACTCTTTGCCGGCGTTGATGCG
11	DKI	330	
24	T10	550	ATGCTACTCTTTGCCGGCGTTGATGGG
			111111111111111111111111111111111111111
10	<b>D3</b>	550	ATGCTACTCTTTGCTGGCGTcGACGGC
9	D1	550	ATGCTACTCTTTGCTGGCGTTGACGGC
14	нкэ	550	ATGCTACTTTTTGCCGGCGTTGATGGG
4.2	mo	330	
15	HK8	550	ATGCTACTGTTTGCCGGCGTTGATGGG
	_		
12	HK3	550	ATGCTACTTTTTGCCGGCGTTGATGGG
	<b>m</b> a	550	CTGCTACTCTTTGCCGGCGTTGATGGG
23	T3	550	CTGCTACTCTTTGCCGGCGTTGATGGG
22	SW2	550	ATGCTACTCTTTGCtGGCGTTGACGGG
	52	550	
17	IND8	550	ATGCTACTCTTTGCCGGCGTTGACGGG
16	IND5	550	ATGCTACTCTTTGCCGGCGTTGACGGG
21	SA10	EEA	ATGCTACTCTTTGCCGGCGTTGACGGG
41	SALU	550	111111111111111111111111111111111111111
20	\$45	550	ATGCTACTCTTTGCCGGCGTTGACGGG
25	US6	550	tTGCTACTCTTTGCCGGCGTTGACGGG
13	HK4	EEA	ATGCTACTCTTTGCCGGCGTTGACGGG
13	AN4	330	111111111111111111111111111111111111111
18	P10	550	ATGCTACTCTTTGCCGGCGTTGACGGa
19	S9	550	ATGCTACTETTTGCtGGtGTTGACGGg
0.05			-mcom> cm-mmcc-cc-cm+c3 -cc-
9-25	consensus		aTGCTACTCTTTGCcGGcGTtGAcGGg

## FIGURE 1C

SEO ID NO:	<u>Isolate</u> T2	1 GCcCAAGTGAgGAACACCAgccgCgGtTACATGGTGACtAACGAC.IGTTCcAATGAgAGCA
27	<b>T4</b>	
28	<b>T9</b>	1 GCCGAAGTGAAGAACACCAGTACCAGCTACATGGTGACAAATGACTGTTCCAACGACAGCA
29	US10	1 GECCARGEGARRACACCAGTACCAGCTALATGGTGACCAATGACTGCTCCAACGACAGCA
26-29	consensus	GCCCAAGTGAagAACACCAgtacCaGCTACATGGTGACCAA-GACTGtTCCAA-GACAGCA
SEO ID NO:	<u>Isolate</u> T2	62 TCACCTGGCAGCTCCAaGCCGCGGTtCTCCACGTCCCCGGGTGTaTCCCGTGtGAGAggct
27	T4	62 TCACETGGCAGCTCCAGGCCGCGGTCCTCCACGTCCCCGGGTGTGTCCCCGTGCGAGABABC
28	<b>T9</b>	62 TCACCTGGCAACTCCAGGCCGCGGTCCTCCACGTCCCCGGGTGCGTCCCGTGCGAGAGAGT
29	US10	62 TCACETGGCAACTEGAGGCEGCGGTCCTCCACGTECCCGGGTGEGTCCCCGTGCGAGAAAGT
26-29	consensus	TCAC-TGGCA-CTccAgGCcGCGCTcCTCCACGTcCCCGGGTGtgTCCCGTGcGAGA-agt
SEO ID NO:	<u>Isolate</u> T2	123 GGGAATACATCeCGaTGCTGGATACCGGTeaCACCAAACGTGGCCGTGCGGCAGCCCGGC
27	T4	123 GGGAATACATCECGGTGCTGGATACCGGTETCACCAAACGTGGCCGTGCGGCAGCCCGGC
28	<b>T9</b>	123 tGGAAAcgCgTCgCGGTGCTGGATACCGGTCTCgCCAAACGTAGCtGTGCAGCGGCCTGGC
29	US10	123 gGGAAAtaCaTCtCGGTGCTGGATACCGGTCTCaCCAAAtGTgGCcGTGCAGCGGCCTGGC
26-29	consensus	gggaaataCatCtCggtGCTgGataCCGGTctCaCCAAAcGTgGCcGTGC-GC-GCC-GGC
SEO ID NO:	Isolate	
26	T2	184 GCtCTtACGCAGGGCTTGCGGACGCACATcGACATGGTTGTGATGTCCGCCACGCTCTGCT
27	T4	184 GCCTCACGCAGGGCTTGCGGACGCACATEGACATGGTTGTGATGTCCGCCACGCTCTGCT
28	<b>T9</b>	184 GCCTCACGCAGGGCTTGCGGACGCACATCGACATGGTTGTGATGTCCGCCACGCTCTGCT
29	<b>US10</b>	184 GCCCTCACGCAGGGCTTGCGGACLCACATCGACATGGTGGTGATGTCCGCCACGCTCTGCT
26-29	consensus	GCcCTcACGCAGGGCTTGCGGACGCACATcGACATGGTLGTGATGTCCGCCACGCTCTGCT
SEO ID NO:		245 CTGCcCTcTACGTGGGGGACCTCTGCGGCGGGGTGATGCTCGCAGCCCAGATGTTCATEGT
26	T2	
27	T4	245 CTGCTCTETACGTGGGGGACCTCTGCGGGGGGTGATGCTCGCAGCCCAGATGTTCATCGT
28	Т9	245 COGCTCTCTACGTGGGGGALCTCTGCGGCGGGGTaATGCTCGCGGCtCAGATGTTCATTaT
29	US10	245 COGCTCTLTACGTGGGGGACLTCTGCGGLGGGATGATGCTCGCAGCCCAAATGTTCATTGT
26-29	consensus	C-GCtCT-TACGTGGGGGAccTCTGCGGcGGGTGATGCTCGCAGCcCAGATGTTCATtgT

## FIGURE 1C

SEO ID NO:	Isolate T2	306 CTCGCCGCgACgcCACTGGTTTGTGCAAGAaTGCAATTGCTCcATCTACCCcGGtACCATC
27	T4	306 CTCGCCGCAACAECACTGGTTTGTGCAAGACTGCAATTGCTCEATCTACCCTTGGCACCATC
28	Т9	306 CTCGCCGCAGCACCACTGGTTGTGCAGGAATGCAACTGCTCCATETACCCTTGGTACCATC
29	US10	306 CTCGCCGCGCACCACTCGTTTGTGCAGGAATGCAACTGCTCCATCTACCCCGGTACCATC
26-29	consensus	CTCGCCGC-aCacCACTgGTTTGTGCA-GAaTGCAA-TGCTCcATcTACCC-GGLACCATC
ero to vo.	Toolata	
SEO ID NO:	<u>Isolate</u> T2	367 ACTGGACACCGTATGGCATGGGACATGATGAACTGGTCGCCCACAGCCACCATGATCC
27	<b>T</b> 4	367 ACTGGACACCGTATGGCATGGGALATGATGATGACTGGTCGCCCACGGCCACCATGATCC
28	<b>T</b> 9	367 ACTGGACACCGTATGGCATGGGACATGATGATGACTGGTCGCCCACAACCACCATGATCL
29	US10	367 ACcGGgCACCGTATGGCATGGGACATGATGATGAACTGGTCGCCCACggCCACttTGATCc
26-29	consensus	ACTGGaCACCGTATGGCATGGGACATGATGAACTGGTCGCCCAC-gCCACcaTGATCc
SEO ID NO:	<u>Isolate</u> T2	428 TGGCGTACGCGATGCGCGTTCCCGAGGTCATCaTAGACATCaTcgGCGGGGCtCACTGGGG
27	T4	428 TGGCGTACGCGATGCGCGTTCCCGAGGTCATC+TAGACATCgTtAGCGGGGCaCACTGGGG
28	<b>T</b> 9	428 TGGCGTACGCGATGCGCGTTCCCGAGGTCATCATAGACATCATCAGCGGAGCCCACTGGGG
29	<b>US10</b>	
26-29	consensus	TGGCGTACGcGATGCGCGTTCCCGAGGTCATCaTAGACATCaT-aGCGGgGCtCAcTGGGG
CEO TO NO.	71	
SEO ID NO:	Isolate T2	489 CGTCATGTT+GGCTTGGCCTACTTCTCTATGCAGGGAGCGTGGGCGAAGGTCATTGTCATC
27	<b>T4</b>	489 CGTCATGTTCGGCTTGGCCTACTTCTCTATGCAGGGAGCGTGGGCGAAAGTCGTTGTCATC
28	<b>T</b> 9	489 CGTCATGTTCGGCCTAGCCTACTTCTCTATGCAGGGAGCGTGGGCGAAGGTCGTTGTCATC
29	US10	489 CGTCLTGTTCGGCLTAGCCTACTTCTCTATGCAGGGAGCGTGGGCGAAAGTCGTTGTCATC
26-29	consensus	CGTCaTGTT6GGCLT-GCCTACTTCTCTATGCAGGGAGCGTGGGCGAA-GTCGTTGTCATC
EEO ID WO.	Isolate	
SEO ID NO:	T2	550 CTC-LTGCTGGCLGCTGGACGCG
27	<b>T</b> 4	550 CTECTGCCGCCGGGGGGGCGCG
28	<b>T</b> 9	550 CrgerdCreaCCGCrisGeGrisGACGCG
29	US10	550 CTECTGCTagCCGCTGGgGTGGACGCG
26-29	consensus	CTt-TGCTggCcGCTGGgGTGGACGCG

## FIGURE 1D

SEO ID NO:	Isolate T8	1	GTGGAAGT±AGAAACAcCAGTT±±AGCTACTACGCCACCAATGATTGCTCgAACAACAGCA
30	DK8	1	GTGGAAGTCAGGAACATCAGTTCCAGCTACTACGCCACCAATGATTGCTCAAACAACAGCA
32	SW3	. 1	GTGGAAGTCAGGAACATCAGTTCTAGCTACTAEGCCACCAATGATTGCTCAAACAGCAGCA
31	DK11	1	GTGGAAGTCAGGAACACCAGTTCTAGLTACTACGCCACCAATGATTGCTCAAACARCAGCA
30-33	consensus		GTGGAAGTCAGGAACA-CAGTTCLAGCTACTACGCCACCAATGATTGCTCaAACAaCAGCA
SEO ID NO:	<u>Isolate</u> T8	62	TCACCTGGCAGCTCACCAACGCAGTTCTCCACCTTCCCGGATGCGTCCCATGTGAGAATGA
30	DK8	62	TCACCTGGCAACTCACCGACGCAGTTCTCCACCTTCCCGGATGCGTCCCATGTGAGAATGA
32	SW3	62	ŤĊŔĊŤĠĠĊŔŔĊŤĊŔĊĊŔŔĊĠĊŔĠŤċĊŦĊĊŔĊĊŦŦĊĊĠĠŔŦĠĊĠŦĊĊĊġŦĠŦĠŔŔĸŦĠŔ
31	DK11	62	TCACCTGGCAACTCACCAACGCAGTLCTCCCACCTTCCCGGATGCGTCCCATGTGAGAATGA
30-33	consensus		TCACCTGGCAGCTCACCAGGCAGTECTCCACCTTCCCGGATGCGTCCCATGTGAGAATGA
SEO ID NO:	<u>Isolate</u> T8	123	CAATGGCACCETGCGCTGCTGGATACAAGTaACACCTAATGTGGCTGTGAAACACCGEGGC
30	DK8	123	CARTGCACCCTGCGCTGCTGGATACAAGTGACACCTAATGTGGCTGTGAAACACCGCGGC
32	SW3	123	+AATGGCACCCTGCACTGCTGGATACAAGTGACACCTAATGTGGCTGTGAAACACCGCGGC
31	DK11	123	CAATGGCACCCTGCACTGCAGGATACAAGTGACACCTAATGTGGCTGTGAAACACCGCGGC
30-33	consensus		CARTGGCACCCTGC-CTGCTGGATACAAGTGACACCTAATGTGGCTGTGAAACACCGcGGC
SEO ID NO:	<u>Isolate</u> T8	184	GCACTCACTCACAACCTGCGAACGCAtGTCGACGTGATCGTAATGGCAGCTACGGTCTGCT
30	DK8	184	GCACTEACTCAEAACCTGCGAACACGTCGACGTGATCGTAATGGCAGCTACGGTCTGCT
32	SW3	184	GCGCTCACTCACAACCTGCGAGCACACGTCGATATGATCGTAATGGCAGCTACGGTCTGCT
31	DK11	184	GCaCTCACTCACAACCTGCGAGCACAEaTaGATATGATEGTAATGGCAGCTACGGTCTGCT
30-33	consensus		GCaCTCACTCACAACCTGCGA-CaCA-gTcGATGATcGTAATGGCAGCTACGGTCTGCT
SEO ID NO	: <u>Isolate</u> T8	245	CGGCCTTGTATGTGGGGGACGTGTGCGGGGCCCGTGATGATAGCGTCGCAGGCTtTCATAAT
30	DK8	245	CGGCCTTGTATGTGGGAGACGTATGCGGGGCCGTGATGATCGTGTCGCAGGCTCTCATAAT
32	SW3	245	CGCCTTGTATGTGGGAGACATGTGCGGGGCCGTGATGATCGTGTCGCAGGCTTTCATAAT
31	DK11	245	CGGCCTGTATGTGGGAGACGTGTGCGGGGCCGTGATGATCGTGTCGCAGGCTTTCATAGT
30-33	consensus		${\tt CGGCCTTGTATGTGGGGGCGTTGTGGGGGCCGTGATGATCGLGTCGCAGGCTLTCATA} {\tt ATTCGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG$

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## FIGURE 1D

SEO ID NO:	<u>Isolate</u> T8	306	ATCGCCaGAACGCCACAACTTCACCCAGGAGTGCAACTGTTCCATCTACCAAGGTCATATC
30	DK8	306	ATCGCCtGAACGCCACAACTTTACCCAGGAGTGCAACTGTTCCATCTACCAAGGTCATATC
32	SW3	306	ATCGCCAGAACGCCACACTITACCCAAGAGTGCAACTGTTCCATCTACCAAGGTCGTATC
• 31	DK11	306	ATCGCCAGAACaCCACCTTTACCCAAGAGTGCAACTGTTCCATCTACCAAGGTCaCATC
30-33	consensus		ATCGCCaGAACgCCACaACTTtACCCA-GAGTGCAACTGTTCCATCTACCAAGGTCatATC
SEO ID NO:	<u>Isolate</u> T8	367	ACCGGCCACCGCATGGCATGGGACATGATGCTGAACTGGTCACCAACTCTCACCATGATCC
30	DK8	367	ACCGGCCACCGCATGGCATGGGACATGATGCTAAACTGGTCACCAACTCTTACCATGATCC
32	SW3	367	ACCGCCACCGCATGGCgTGGGACATGATGCTAAACTGGTCACCAACTCTTACCATGATCC
31	DK11	367	ACCGGCCACCGCATGGCATGGGACATGATGCTLAACTGGTCACCAACTCTCACCATGATCC
30-33	consensus		ACCGGCCACCGCATGGCATGGGACATGATGCTAAACTGGTCACCAACTCT-ACCATGATCC
SEO ID NO:	<u>Isolate</u>		
33	<b>T8</b>		TCGCCTAcGCtGCTGTGTGCCTGAACTAGtCCTtgAaGTTGTCTTCGGCGGCCATTGGGG
30	DK8		TCGCCTATGCCGCTCGTGTTCCTGAGCTAGCCCTccAgGTTGTCTTCGGCGGCCATTGGGG
32	SW3		TEGCCTATGCCGCTCGTGTTCCTGAGCTAGTCCTTGAAGTTGTCTTCGGCGGCCATTGGGG
31	DK11	428	ŤeĠĊĊŤŔŤĠĊĊĠĊeĊĠŤĠŤŤĊĊŤĠŔĠĊŤŔĠŤĊĊŤŤĠŔŔĠŦĸĠŦĊŦŦĊĠĠŧĠĠŧĊĸŦŢĠĠĠ
30-33	consensus		Tegectatgeegetegtgtectgagetagtecttgaagttgtettteggeggeeattggg
SEO ID NO:	<u>Isolate</u> T8	489	CGTGGTGTTTGGCTTGGCCTATTTCTCCATGCAAGGAGCGTGGGCCAAAGTCATCGCCATC
30	DK8	489	CGTGGTGTTTGGCTTGGCCTATTTCTCCATGCAGGGAGCGTGGGCCAAAGTCATTGCCATC
32	SW3	489	CGTGGTGTTTGGCTTGGCCTATTTCTCCATGCAaGGAGCGTGGGCCAAGGTCATTGCCATC
31	DK11	489	EGTGGTGTTTGGCCTATTTCTCCATGCAgGGAGCGTGGGCCAAGGTCATTGCCATC
30-33	consensus		cGTGGTGTTTGGCTTGGCCTATTTCTCCATGCA-GGAGCGTGGGCCAA-GTCATEGCCATC
SEO ID NO:	<u>Isolate</u> T8	550	CTCCTcCTTGTCGCAGGAGTGGAcGCA
30	DK8	550	CTCCT+CTIGTCGCAGGAGTGGATGCA
, 32	SW3	550	ctcctgctigtcgcaggagtggatgca
31	DK11	550	CTCCT+CTTGTaGCAGGAGTGGATGCA
. 30-33	consensus		CTCCTtCTTGTcGCAGGAGTGGAtGCA

#### FIGURE 1E

SEO ID	NO: <u>Isolate</u> DK12	1	tagagtggcggaatgtgtccggcctctacgtccttaccaacgactgttccaatagcagta
- 36	HK10	1	CTAGAGTGGCGGAATGTCTGGCCTCTATGTCCTTACCAACGACTGTCCCAATAGCAGTA
37	<b>S2</b>	1	CTAGAGTGGCGGAATACGTCTGGCCTCTATGTCCTCACCAACGACTGTTCCAATAGCAGTA
. 39	S54	1	CTAGAGTGGCGGAATACGTCTGGCCTCTATaTCCTTACCAACGACTGTTCCAATAGCAGTA
38	S52	1	CTAGAGTGGCGGAATACGTCTGGCCTCTATGTCCTTACCAACGACTGTTCCAATAGCAGTA
35-39	consensus		CTAGAGTGGCGGAATACGTCtGGCCTCTAtgTCCTtACCAACGACTGTtCCAATAGCAGTA
SEO ID 1	NO: Isolate		
35	DK12	62	Tegrgtatgaggccgatgacgtcattctgcacacctggctgtgtaccttgtgttcagga
36	HK10	62	TTGTGTATGAGGCCGATGACGTCATTCTGCACACCTGGCTGTGTACCTTGTGTTCAGGA
37	S2	62	TIGIGTATGAGGCCGATGACGTLATTCTGCACACCCTGGCTGTGTACCTTGTGTTCAGGA
39	S54	62	TTGTGTATGAGGCCGATGACGTCATTCTGCACACCCGGCTGTGTACCTTGTGTTCAGGA
38	<b>S</b> 52	62	TTGTGTATGAGGCCGATGACGTCATTCTGCACACCCCGGCTGTGTACCTTGTGTTCAGGA
35-39	consensus		TEGTGTATGAGGCCGATGACGTCATTCTGCACACACCEGGCTGTGTACCTTGTGTTCAGGA
SEO ID	NO: Isolate		
SEO ID	NO: Isolate DK12	123	CGGCAATACATCLACGTGCTGGACCTCAGTGACGCCTACAGTGGCAGTCAGGTACGTCGGA
			CGGCAATACATCCACGTGCTGGACCTCGGTGACACCTACAGTGGCAGTCAGGTACGTCGGA
35	DK12	123	CGGCAATACATCCACGTGCTGGACCTCGGTGACACCTACAGTGGCAGTCAGGTACGTCGGA
35 36	DK12 HK10	123 123	CGGCAATACATCCACGTGCTGGACCCCAGTGACACCTACAGTGGCAGTCAGGTACGTCGGA
35 36 37	DK12 HK10 S2	123 123 123	CGGCAATACATCCACGTGCTGGACCTCGGTGACACCTACAGTGGCAGTCAGGTACGTCGGA
35 36 37 39	DK12 HK10 S2 S54	123 123 123	CGGCAATACATCCACGTGCTGGACCTCGGTGACACCTACAGTGGCAGTCAGGTACGTCGGA
35 36 37 39 38 35-39	DK12 HK10 S2 S54 S52 consensus	123 123 123 123	CGGCAATACATCCACGTGCTGGACCTCGGTGACACCTACAGTGGCAGTCAGGTACGTCGGA
35 36 37 39 38	DK12 HK10 S2 S54 S52 consensus	123 123 123 123	CGGCAATACATCCACGTGCTGGACCTCGGTGACACCTACAGTGGCAGTCAGGTACGTCGGA
35 36 37 39 38 35-39	DK12 HK10 S2 S54 S52 Consensus NO: Isolate	123 123 123 123	CGGCAATACATCCACGTGCTGGACCTCGGTGACACCTACAGTGGCAGTCAGGTACGTCGGA
35 36 37 39 38 35-39 SEO ID	DK12 HK10 S2 S54 S52 Consensus NO: Isolate DK12	123 123 123 123 184	CGGCAATACATCCACGTGCTGGACCTCGGTGACACCTACAGTGGCAGTCAGGTACGTCGGA
35 36 37 39 38 35-39 SEO ID 3	DK12 HK10 S2 S54 S52 Consensus NO: Isolate DK12 HK10	123 123 123 123 184 184 184	CGGCAATACATCCACGTGCTGGACCTCGGTGACACCTACAGTGGCAGTCAGGTACGTCGGA
35 36 37 39 38 35-39 SEO ID 35 36 37	DK12 HK10 S2 S54 S52 Consensus NO: Isolate DK12 HK10 S2	123 123 123 123 184 184 184	CGGCAATACATCCACGTGCTGGACCTCGGTGACACCTACAGTGGCAGTCAGGTACGTCGGA

## FIGURE 1E

SEO ID	NO: <u>Isolate</u> DK12	245	CTGCGCTCTACGTGGGtGATgTGTGTGGGGCCGTCTTCCTtGTGGGACAAGCCTTCACGTT
36	HK10	245	CTGCGCTCTACGTGGGGGATATGTGTGGGGCCGTCTTCCTCGTGGGACAAGCCTTCACGTT
37	<b>S2</b>		CTGCGCTCTACGTGGGTGATATGTGTGGGGCCGTCTTTCTCGTGGGACAAGCCTTCACGTT
, 39	\$54		CIGCGCTCTATGTGGGGGGCCGTCTTTCTCGTGGGACAAGCCTTCACGTT
38	S52	245	CTGCGCTCTATGTGGGGGCCGTCTTTCTCGTGGGACAAGCCTTCACGTT
35-39	consensus		CTGCGCTCTAcGTGGGGCGATATGTGTGGGGCCGTCTTtCTcGTGGGACAAGCCTTCACGTT
	_		
SEO ID		206	CAGACCECGTCGCCATCAAACaGTCCAGACCTGTAACTGCTCGCTGTACCCAGGCCAECTT
35	DK12		
36	HK10	306	CAGACCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
37	S2	306	CAGACCTCGTCGCCATCAAACCGTCCAGACCTGTAACTGCTCGCTGTACCCAGGCCATCTT
39	S54	306	CAGACCTCGTCGCCATCAAACGGTCCAGACCTGTAACTGCTCGCTGTACCCCAGGCCATCTT
38	S52	306	CAGACCTCGTCGCCATCAAACGGTCCAGACCTGTAACTGCTCGCTGTACCCAGGCCATgTT
35-39	consensus		CAGACCECGTCGCCATCAAACGGTCCAGACCTGTAACTGCTCGCTGTACCCAGGCCAECTT
SEO ID	NO: Isolate		
35	DK12	367	TCAGGACATCGAATGGCTTGGGATATGATGATGATTGGTCCCCCGCLGTGGGTATGGTGG
-	DK1.2		
35 36		367	TCAGGACATCGAATGGCTTGGGATATGATGATGAATTGGTCCCCCGCGTGGGTATGGTGG
-	DK1.2	367	TCAGGACATCGCATGGCTTGGGATATGATGATGATTGGTCCCCCGCCTGGGTATGGTGG  TCAGGACATCGCATGGCTTGGGATATGATGATGATGATTGGTCCCCCGCTGTGGGTATGGTGG  TCAGGACATCGCATGGCTTGGGATATGATGATGATTGATCCCCCCGCTGTGGGTATGGTGG
36 37	DK1.2 HK1.0 S2	367 367	TCAGGACATCGAATGGCTTGGGATATGATGATGATTGGTCCCCCGCCGTGGGTATGGTGG
36	DK1.2 HK1.0 S2 S54	367 367 367	TCAGGACATCGCATGGCTTGGGATATGATGATGATTGGTCCCCCGCCGTGGGTATGGTGG
36 37	DK1.2 HK1.0 S2	367 367 367	TCAGGACATCGAATGGCTTGGGATATGATGATGATTGGTCCCCCGCCGTGGGTATGGTGG
36 37 39	DK1.2 HK1.0 S2 S54	367 367 367	TCAGGACATCGCATGGCTTGGGATATGATGATGATTGGTCCCCCGCCGTGGGTATGGTGG
36 37 39 38	DK1.2 HK1.0 S2 S54 S52	367 367 367	TCAGGACATCGAATGGCTTGGGATATGATGATGATTGGTCCCCCGCGTGGGTATGGTGG
36 37 39 38 35-39	DK12 HK10 S2 S54 S52 Consensus	367 367 367	TCAGGACATCGAATGGCTTGGGATATGATGATGATTGGTCCCCCGCCGTGGGTATGGTGG
36 37 39 38	DK12 HK10 S2 S54 S52 Consensus	367 367 367	TCAGGACATCGAATGGCTTGGGATATGATGATGATTGGTCCCCCGCCGTGGGTATGGTGG
36 37 39 38 35-39 SEO ID	DK12 HK10 S2 S54 S52 consensus NO: Isolate DK12	367 367 367 367	TCAGGACATCGAATGGCTTGGGATATGATGATGATTGGTCCCCCGCCGTGGGTATGGTGG
36 37 39 38 35-39	DK12 HK10 S2 S54 S52 consensus	367 367 367 367 428	TCAGGACATCGAATGGCTTGGGATATGATGATGATTGGTCCCCCGCCGTGGGTATGGTGG
36 37 39 38 35-39 SEO ID	DK12 HK10 S2 S54 S52 consensus NO: Isolate DK12	367 367 367 367 428	TCAGGACATCGAATGGCTTGGGATATGATGATGATTGGTCCCCCGCCGTGGGTATGGTGG
36 37 39 38 35-39 SEO ID 35 36 37	DK12 HK10 S2 S54 S52 consensus NO: Isolate DK12 HK10 S2	367 367 367 367 428 428	TCAGGACATCGAATGGCTTGGGATATGATGATGATTGGTCCCCCGCCGTGGGTATGGTGG
36 37 39 38 35-39 SEO ID 35	DK12 HK10 S2 S54 S52 CONSENSUS NO: Isolate DK12 HK10	367 367 367 367 428 428 428	TCAGGACATCGAATGGCTTGGGATATGATGATGATTGGTCCCCCGCCGTGGGTATGGTGG
36 37 39 38 35-39 SEO ID 35 36 37	DK12 HK10 S2 S54 S52 consensus NO: Isolate DK12 HK10 S2	367 367 367 367 428 428 428	TCAGGACATCGAATGGCTTGGGATATGATGATGATTGGTCCCCCGCCGTGGGTATGGTGG

#### FIGURE 1E

SEO ID NO	): <u>Isolate</u> DK12	489	CATCaTGGCgGGCCTAGCCTATTACTCCATGCAGGGCAACTGGGCCAAGGTCGCTATCATC
. 36	HR(10	489	
37	S2	489	CATCTTGGCGGGCCTAGCCTATTACTCCATGCAAGGCAACTGGGCCAAGGTCGCTATCATC
, 39	S5 <b>4</b>	489	ĊĂŢĊŢŢĠĊĠĠĠĊĊŢŔĠĊĊŢŔŢŢŔŢŢĊŢŔŢĠĊŔĠĠĠĊŔŔĊŢĠĠĊĊŔŔĠĠŢĊĠĊŢŔŢĊŔŢĊ
38	S52	489	CATCHTGGCGGGCCTAGCCTATTATTCTATGCAGGGCCAACTGGGCCAAGGTCGCTATtgTC
35-39	consensus		CATCHTGGCgGGCCTAGCCTATTACTCCATGCAGGGCCAACTGGGCCAAGGTCGCTATCATC
SEO ID NO	: <u>Isolate</u> DK12	550	ATGGTTATGTTTCAGGAGTCGATGCC
			11111111111111111111111111111111
36	HKT0	550	ATGGTTATGTTTCAGGGGTCGATGCC
36 37	HK10 S2		ATGGTTATGTTTTCAGGGGTCGATGCC
_		550	
37	<b>S2</b>	550 550	ATGGTTATGTTTTCAGGGGTCGACGCC

#### FIGURE 1F

SEC ID NO: Isolate	
43 27	1 GTCAACTATCaCAATGCCTCGGGCGTCTATCACATCACCAACGACTGCCCGAACTCGAGCA
. 42 Z6	
42-43 consensus (Z6)	GTEAACTATCGCAATGCCTCGGGCGTCTATCACGTCACCAACGACTGCCCGAACTCGAGCA
•	
SEO ID NO: Isolate	62 TAZTGTATGAGGCCGAACACCACATCCTACACCTCCCAGGGTGCGTACCCTGTGTGAGGGA
. 43	
42 Z6	62 TAGTGTATGAGGCCGAACACCAGATCTTACACCTCCCAGGGTGCETGCCCTGTGTGAGGGE
42-43 consensus (Z6)	TAGTGTATGAGGCCGAACACCAGATCLTACACCTCCCAGGGTGCLTGCCCTGTGTGAGGGL
SEO ID NO: Isolate	
43 Z7	123 gGGGAACCAGTCACGCTGCTGGGTGGCCCTTACTCCCACCGTGGCGGCGCCTTATATCGGT
<b>42</b> Z6	123 tGGGAAtCAGTCACGCTGCTGGGTGGCCCTTACTCCCACCGTGGCGGtGtCTTATATCGGT
•	•
42-43 consensus (Z6)	tgggaatcaggtgctggtggcccttactcccaccgtggcggtgtcttatatcggt
SEO ID NO: Isolate	
43 27	184 GCACCGCTTGAATCCATCCGGAGACATGTGGACCTGATGGTAGGCGCtGCTACAGTGTGCT
42 76	
<b>42 Z</b> 6	184 GCTCCGCTTGAcTCCcTCCGGAGACATGTGGACCTGATGGTGGGCGCCGCTACTGTaTGCT
42-43 consensus (26)	GCtCCGCTTGAcTCCcTCCGGAGACATGTGGACCTGATGGTgGGCGCcGCTACtGTaTGCT
CEO TR NO. Teologo	
SEO ID NO: Isolate	245 CcGCtCTCTACaTTGGGGACCTGTGCGGTGGcGtATTtTTGGTTGGtCAGATGTTtTCTTT
<b>4</b> 2 <b>Z</b> 6	245 CtGCCCTCTACgTTGGAGAtCTGTGCGGTGGTGCATTCTTGGTTGGCCAGATGTTCTCCTT
42-43 consensus (Z6)	CtGCCCTCTACgTTGGaGAtCTGTGCGGTGGtGcATTCTTGGTTGGcCAGATGTTcTCcTT
,,	_
SEO ID NO: Isolate	
43 27	306 CCAGCCGCGACGCCACTGGACTACGCAGGACTGCAATTGTTCCATCTAtGCgGGGCAcgTt
<b>4</b> 2 <b>Z</b> 6	306 CCAGCCGCGACGCCACTGGACTACGCAGGACTGCAATTGTTCLATCTACGCAGGGCATATC
42-43 consensus (26)	CCAGCCGCGACGCCACTGGACTACGCAGGACTGCAATTGTTCLATCTACGCAGGGCALATC
SEO ID NO: Isolate	
43 27	367 ACAGGCCACAGAATGGCATGGGACATGATGAACTGGAGTCCCACAACCACCLTGgTCC
42 Z6	367 ACGGGCCACAGGATGGCATGGGACATGATGAACTGGAGTCCCACAACCACCCTGCTEC
42-43 consensus (Z6)	ACGGGCCACAGGATGGCATGGGACATGATGAACTGGAGTCCCACAACCACCCTGcTtC

#### FIGURE 1F

SEO ID NO: Iso		428	TOGCCCASGTLATGAGGATCCCTAGCACTCTGGTgGACCTACTCACTGGAGGGCACTGGGG
42	<b>Z</b> 6	428	TCGCCCAGGTCATGAGGATCCCTAGCACTCTGGTAGAtCTACTCGCTGGAGGGCACTGGGG
42-43 consensus	(26)		TOGCCCAGGT-ATGAGGATCCCTAGCACTCTGGTaGAtCTACTCGCTGGAGGGCACTGGGG
SRO ID NO: Isol		489	tatccitateggggtgcatacitctgcatgcaagctaattgggccaaggtcattctggtc
42	<b>Z</b> 6	489	CgTCCTTGTTGGGCTGCCTACTTCAGtATGCAAGCTAATTGGGCCAAaGTCATCCTGGTC
42-43 consensus	(Z6)		cgTCCTTgTtGGGtTGGCgTACTTCaGtATGCAAGCTAATTGGGCCAAaGTCATcCTGGTC
SEO ID NO: Isol		550	CTTTTCCTCTaCGCTGGAGTTGATGCC
42	<b>26</b> 5	550	CTTTTCCTCTCGCTGGAGTTGATGCC
42-43 consensus	(Z6)		CTTTTCCTCTECGCTGGAGTTGATGCC

#### FIGURE 1G

SRO ID NO: 45  47  49  46  50  48	: Isolate SA1 SA5 SA7 SA4 SA13	1 GTtCCCTACCGGAATGCCTCTGGGGTTTAcCATGTCACCAATGACTGCCCAAACTCCTCCA 1
45-50	consensus	GTECCCTACCGAAAEGCCTCEGGGGTETAECATGTCACCAATGAETGCCCAAACTCETCCA
SEO ID NO:	: Isolate	
45	SAI	62 TAGTCTACGAGGCTGATAGCCTGATCTTGCACGCACCTGGCTGCCTGTGTCAGGCA
47	SA5	62 TAGTCTACGAGGCTGATAACCTGATECTGCACGCACCTGGTTGCGTGCCCTGTGTCAAGGA
49	SA7	62 TAGTCTA+GAGGCTGA-CACCTGATCCTGCACGCACCTGGTTGCGTGCCCTGTGTCAGaCA
46	SA4	62 TAGTETACGAGGCTGATAACCTGATCTTGCAEGCACCTGGTTGCGTGCCETGTGTCAGGCA
50	SA13	62 Tegtctacgaggctgatgacctgatcttacacgcacctggttgcgtgccctgtgttaggca
45	22.6	
48	SA6	62 TEGICIAEGAGGCIGATGACCIGATCCIACACGCACCIGGCIGCCCIGIGICCGGAA
45-50	consensus	Tagtctacgaggctgataacctgatc-tgcacgcacctggttgcgtgccctgtgtcaggca
SEO ID NO:	<u> Isolate</u>	
45	SA1	123 AGATAATGTCAGTAGGTGCTGGGTCCAAATCACCCCCACACTGTCAGCCCCGACCLTCGGA
47	SAS	123 AGGTAATGTCAGTAGGTGCTGGGTCCAAATCACCCCCACATTGTCAGCCCCGAACCTCGGA
49	SA7	123 ABATRATGTCAGTAGGTGCTGGGTCCAAATCACCCCCACATTGTCAGCCCCGAACCTCGGA
46	SA4	123 AGATAATGTCAGTAaGTGCTGGGTCCAAATCACCCCCACGTTGTCAGCCCCGAAtCTCGGA
50	6213	123 GGGTAATGTCAGTAGGTGCTGGGTCCAGATCACCCCCACACTGTCAGCCCCCGAGCCTCGGA
30	SA13	
48	SA6	123 GGATAATGTCAGTAGATGCTGGGTLCALATCACCCCCACACTATCAGCCCCGAGCCTCGGA
45-50	consensus	agataatgtcagtaggtgctgggtccaaatcaccccaca-tgtcagccccgaacctcgga

## FIGURE 1G

SEO ID NO:	<u>Isolate</u> SA1	184 GCGGTCACGGCTCCTCTTCGGAGGGCCGTTGACTACTTAGCGGGAGGAGCTGCtCTCTGCT
47	SAS	
	SA7	184 GCGTCACGGCTCCTCTTCGGAGGGCCGTTGACTAGCGGGAGGGGCTGCCCTCTGCT
49		184 GCGGTCACGGCTCCTCTCGGAGGGCCGTTGACTTAGCGGGAGGGGCCTGCCCTCTGCT
46	SA4	
50	SA13	184 ĠĊĠĠŤĊŔĊĠĠĊŤĊĊŤĊŦŤĊĠĠŔĠĠĊĊĠŦŤĠŔĊŦŔĊŦŤŔĠĊĠĠĠĠĠĠĠĠĊŦĠĊĊŦĿŦĠĊŦ
48	SA6	184 GCGGTCACGGCTCCTCTTCGGAGGGCCGTTGALTACTTGGCGGGGGGGGGG
45-50	consensus	GCGGTCACGGCTCCTCTTCGGAGGGcCGTTGAcTACtTaGCGGGGGGGGGCtGCcCTcTGCT
SEO ID NO:		245 CCGCACTATACGTCGGcGACGCGTGCGGGGGCAGTGTTLcTGGTAGGCCAAATGTTCACCTA
45	SAL	111111111111111111111111111111111111111
47	SA5	245 CCGCACTATACGTCGGGGACGCGTGCGGGGCAGTGTTCTTGGTAGGCCAAATGTTCACCTA
49	SA7	245 CCCCCTATACGTCGGGGACGCGTGCGGGGCAGTGTTTTTGGTAGGCCAGATGTTCAGCTA
46	SA4	245 CCGCaCTATACGTCGGGGACGCGTGCGGGGCAGTGTTTTTGGTAGGCCAAATGTTCACCTA
50	SA13	245 CCGCGTTÁTÁCGTCGGAGÁCGCGTGCGGGGCÁGTGTTTTTGGTÁGGLCÁÁÁTGTTCÁCCTÁ 
48	SA6	245 CCGCGTTATACGTCGGAGACGEGTGCGGGGCAETGTTTTTGGTAGGCCAAATGTTCACCTA
45-50	consensus	CCGC-CTATACGTCGGGGACGCGTGCGGGGCAGTGTTLLTGGTAGGCCA2ATGTTCACCTA
SEO ID NO:	<u> Isolate</u>	·
45	SAI	306 TAGGCCTCGCCAGCATACcACAGTGCAGGACTGCAACTGTTCCATTTACAGtGGCCATATC
47	SA5	306 TAGGCCTCGCCAGCATACTACGGTGCAGGACTGCAACTGTTCCATTTACAGGGGCCATATC
40	SA7	
49	SA/	
46	SA4	306 TÁGGCCTCGCCÁGCÁCACTÁCGGTGCÁAGÁCTGCÁÁLTGCTCLÁTTTACAGTGGCCATÁTC
50	SA13	306 ŤÁĠĊĊŤĊĠĊĊĠĠĊÁŤÁĸŤgŧŧĠŤĠĊÁĠĠĂĊŤĠĊÁÁĊŤĠŧŤĊCATŦŦĀCAGTGGCCAcATC
48	SA6	
45-50	consensus	TAGGCCTCGCCAGCAtactacgGTgCAgGACTGCAAcTGtTCcATTTACAGtGGCCAtATC
SEO ID NO:	<u> Isolate</u>	
45	SAI	367 ACCGGCCACCGGATGGCtTGGGACATGATGATTGGTCACCTACGACAGCCTTGcTGA
47	SA5	367 BCCCCCCACCGAATGCCATGGGACATGATGATTGATTGCTCACCTACGACAGCCTTGGTGA
49	SA7	367 ACCGGCCACCGAATGGCATGGGACATGATGATGATTGGTCACCTACGACAGCCTTGGTGA
46	SA4	367 ACCGCCACCGGATGGCATGGACATGATGATTGGTCACCTACGACGGCCTTGCTGA
50	SA13	367 ACCGGCCACCGGATGGCATGGGACATGATGATTGGTCACCTACAACAGCETTGGTGA
48	SA6	
45-50	consensus	ACcGGCCACCGGATGGCATGGCACATGATGATGAATTGGTCACCtaCgACaGCcTTGgTGA

45-50 consensus

26/47

## FIGURE 1G

SEO ID NO:	Isolate		
45	SAI	428	TGGCCCAGaTGCTACGGATcCCCCAgGTGGTCATaGACATCATaGCCGGGGGCCACTGGGG
47	SA5	428	TGGCCCAGgTGCTACGGATTCCCCAaGTGGTCATEGACATCATTGCCGGGGCCCACTGGGG
49	SA7	428	TGGCCCAGTTGCTACGGATTCCCCAGGTGGTCATCGACATCATTGCCGGGGCCACTGGGG
	63.4	400	
46	SA4	4.25	TGGCCCAGTTGCTACGGATTCCCCAGGTGGTCATCGACATCATTGCCGGGGGCCACTGGGG
50	SA13	428	TGGCCCAGTTGtTACGGATTCCCCAGGTGGTCATTGACATCATTGCCGGGGcCCACTGGGG
30	3413	420	TGGCCCAGTTGCTACGGATTCCCCAGGTGGTCATTGACATCATTGCCGGGGCCCACTGGGG
48	SA6	428	TGGCCCAaaTGcTACGGATTCCCCAGGTGGTCATTGACATCATTGCCGGGGGCCACTGGGG
			10000 100000000000000000000000000000000
45-50	consensus		TGGCCCAgeTGcTACGGATeCCCCAgGTGGTCATEGACATCATEGCCGGGGGCCACTGGGG
			•
SEO ID NO:	<u> Isolate</u>		
45	SAI	489	GGTCTTGTTtGCCGCCGCATACTTtGCGTCgGCCGCCAACTGGGCTAAGGTAGTGCTGGTt
47	SA5	489	GGTCTTGTTCGCCGCCATACTTCGCGTCAGCGGCTAACTGGGCTAAGGTTGTGCTGGTC
49	SA7	489	
43	SA	489	GGTCTTGTTCGCCGCCGCATATTTCGCGTCAGCGGCTAACTGGGCTAAGGTTGTGCTGGTC
46	SA4	ARG	GGTCTTGTTtGCCGCCGCATATTTCGCGTCAGCGGCTAACTGGGCTAAGGTTaTaCTGGTC
	-	107	
50	SA13	489	GGTCTTGTTCGCCGCCGCATACTaCGCGTCGGCGGCTAACTGGGCCAAGGTTGTGCTGGTC
48	SA6	489	GGTCTTGTTCGCCGCLGCATACTLCGCGTCGGCGGCTAACTGGGCLAAGGTTGTGCTGGTC
45-50	consensus		GGTCTTGTTcGCCGccGCATAcTtcGCGTC-GCgGCtAACTGGGCtAAGGTtgTgCTGGTc
SEO ID NO:	Isolate		
45	SA1	550	CTGTT-CTGTTTGCGGGGGTCGATGGC
••		550	1111 11111111111111111
47	SA5	550	CTGTTTCTGTTTGCGGGGGTCGATGGC
49	SA7	550	TTGTTTCTGTTTGCGGGGGTCGATGCC
46	SA4	550	TTGTTTCTGTTTGCGGGGGTCGATGCC
	05.5		
50	SA13	550	CIGITICIGE TIGUEGGGGTCGATGCC
48	SA6	EEC	ttgtttctgtttgcggggttgatgcc
40	SAG	330	C1G111C1G1 11GCGGGGGG LGM1GCC

-TGTTtCTGTTTGCGGGGGTcGATGcC

## FIGURE 1H

SEO ID NO:	Genotype							
30-33	(IV/2b)	1	<b>GTGGAAGTCAGGAACAtCAGTTC</b>	LAGCTACI	'ACGCCACC	AATGA	ITGCTCa	AACAaCAGCA
34	(2c)	1	<b>GTGGAGGTCAAGGACACCGGCGA</b>	CTCCTACX	TGCCGACC	'AACGA'	TTGCTCC	AACTCTAGTA
26-29	(III/2a)	1	GCCCAAGTGAagAACACCAgtac	CaGcTAcA	TGGTGAC	:AAcGA(	TGtTCc	AAtGAcagca
. 35-39	(V/3a)	1	CTAGAGTGGCGGAATACGTCtGG	CTCTAte	TCCTtACC	'AACGA	TGTtCC	AATAGCAGTA
9-25	(II/1b)	1	<b>tAtGAaGTGCgCAACGTgTCCGG</b>	SgtgTAcc	AtGTCACo	AACGA	TGCTCC	AACTcaAGca
1-8	(I/la)	1	<b>tACCAAGTGCGCAACTCcaCgGG</b>	CTTTACC	'ATGTCACC	AATGA	TGCCCT	AACTCGAGLA
, 40.	(4a)	1	GAGCACTACCGGAATGCTTCGGG	CATCTATO	ACATCACO	'AATGA'	FTGTCCG	AATTCCAGTA
42-43	(4c)	1	<b>GTTAACTATCGCAATGCCTCGGG</b>	CGTCTATC	ACGTCACC	'AACGA(	TGCCCG	AACTCGAGCA
44	(4d)	1	TACAACTATCGCAACAGCTCGGG	<b>IGTCTACC</b>	ATGTCACC	'AACGA'	PTGCCCG	AACTCGAGCA
41	(4b)	1	GTGCACTACCGGAATGCTTCGGG	GTCTATO	ATGTCACO	AATGA	TGCCCT	AACACCAGCA
45-50	(5a)	1	<b>GTtCCcTACCGaAAtGCCTCtGG</b>	GTETALO	ATGTCACC	AATGA	TGCCCa	AACTCETCCA
51	(6a)	1	CITACCTACGGCAACTCCAGTGG	SCTATACO	ATCTCACA	AATGAT	TGCCCC	AACTCCAGCA
	• • •							
1-51	consensus		A	TA	AC A	A GA 1	rg Ca	A
SEO ID NO:	Genotype							
30-33	(IV/2b)	62	TCACCTGGCAaCTCACCaACGCA	FTECTCCA	CCTTCCCG	GATGC	FTCCCat	GTGAGAATGA
34	(2c)	62	TCGTTTGGCAGCTTGAAGGAGCA	FIGCTICA	TACTCCTG	GATGC	TCCCTT	GTGAGCGTAC
26-29	(III/2a)	62	TCACCTGGCAACTCCAgGCCGCG	TCCTCCA	CGTcCCCG	GGTGtg	TCCCGT	GcGAGAaagt
35-39	(V/3a)	62	TEGTGTATGAGGCCGATGACGTC	ATTCTGCA	CACACCEG	GCTGTG	TACCTTY	GTGTTCAGGA
9-25	(II/1b)	62	TtGTGTatGAggCAgcgGACaTG	<b>ITCATGCA</b>	CACCCCCG	GgTGcg	TGCCCN	GcGTtCgGGA
1-8	(I/1a)	62	TEGTGTACGAGGCGGCGGATGCc	TCCTGCA	caCtCCgG	GGTGTG	TCCCTI	GCGTTCGcGA
40	(4a)	62	TAGTCTATGAAGCTGACCATCAC	<b>ITCCTACA</b>	CTTGCCGG	GGTGCG	TACCCIN	GTGTGATGAC
42-43	(4c)	62	TAGTGTATGAGGCCGAACACCAG	ITCETACA	CCTCCCAG	GGTGCt	TgCCCT	GTGTGAGGGt
44	(4d)	62	TAGTCTATGAAACCGATTACCAC	TCTTACA	CCTCCCGG	GATGCG	TTCCTT	GCGTGAGGGA
41	(4b)	62	TAGTGTACGAGACGGAGCACCAC	LTCATGCA	CTTGCCAG	GGTGTG	TCCCCT	GTGTGCGGAC
45-50	(5a)	62	TagtctacgaggCtgataaCCTgi	TCLTgCA	CGCACCTG	GtTGCG	TGCCcT	GTGTcaggcA
51	(6a)	62	TCGTGCTGGAGGCGGATGCTATG	LTCTTGCA	TTTGCCTG	GATGCI	TGCCTT	GTGTGAGGGT
1-51	consensus		A T	T T CA	. CC G	G TG	T CC T	G G
SEO ID NO:			->>mcca>ca-mca-maamaa			memeee		N C N C C C C C C C
30-33	(IV/2b)		caatggcaccctgcgctgctgga: cgccaacgtctctcgatgttggg:					
34	(2c)	123	gGGAAAtaCaTCtCGATGTTGGG.					
26-29	(III/2a)	123						
35-39	(V/3a)	123	CGGCAATACATCCACGTGCTGGA					
9-25	(II/1b)	123	gaacAActcCTCccgcTGcTGGG					
1-8	(I/1a)	123	GGgTaaCgcctCGAggTGTTGGG:					
40	(4a)		TGGGAACACATCGCGTTGCTGGA( EGGGAAECAGTCACGCTGCTGGG					
42-43	(4c)		EGGGAAECAGTCTACATGCTGGG AGGGAACAAGTCTACATGCTGGG					
44	(4d)		AGGGAACAAGTCTACATGCTGGG. GGAGAATACTTCTCGCTGCTGGG.					
41	(4b)							
45-50	(5a)	123	agaTAATGTCAGTAggTGCTGGG			_		
51	(6a)	123	CGATGATCGGTCCACCTGTTGGC	11001016	melliche	100	.CAIACCI	MANIGCT TCC
1-51	consensus		TG TGG	T	C CC A	тс	•	
T-3T	-motnong		19 199	-	CCA		•	

## FIGURE 1H

SEO ID NO:	<u>Genotype</u>		
30-33	(IV/2b)	184	GCaCTcACTCAcAACCTGCGAaCaCAtgTcGAcaTGATcGTAATGGCAGCTACGGTCTGCT
34	(2c)	184	GCTCTCACTAAGGGCCTGCGAGCACACCATCGATATCATCGTGATGTCTGCTACGGTCTGTT
26-29	(III/2a)	184	GCcCTcACGCAGGCTTGCGGACGCACATCGACATGGTtGTGATGTCCGCCACGCTCTGCT
35-39	(V/3a)	184	GCAACCACCGCLTCGATACGCAGTCATGTGGACCTALTAGTGGGCGCGGCCACGATGTGCT
9-25	(II/1b)	184	off concrete action of the contract of the con
1-8	(I/la)	3.84	TTCCcccCacCGCAcCTtCGACGTCACATCGAtCTGCTtGTCGGGAAGCGCCACCCTCTGCT
	(4a)	184	GCTCCGCTTGAGTCGTTCCGGCGACATGTGGACTTAATGGTAGGCGCGGCCACTTTGTGTT
40		104	GCtCCGCTTGAcTCCcTCCGGAGACATGTGGACCTGATGGTGGGCGCCGCTACtGTaTGCT
42-43	(4c)	104	GCTCCGCTTGAGTCTTTGAGACGTCACGTGGATCTGATGGTGGGCGGCGCCACTCTCTGCT
44	(4d)	164	GCACCGTTAGAGTCCATGCGCAGGCATGTAGACCTGATGGTGGGTG
41	(4b)	184	GCGCTCACGGCTCCTCTTCGGAGGGCCGTTGAcTACtTaGCGGGaGGGGCtGCcCTCTGCT
45-50	(5a)	184	ACCCCCCAACGCATTCCGCAGCATGTGGATCTTCTTGCGGGCGCCGCAGTGGTTTGCT
51	(6a)	184	ACCCCCCAACGCGATTCCGCAGGCATGTGGATCTTCTTGCGGGCGCCGCAGTGGTTTGCT
			T G T GA T G GC T TG T
1-51	consensus		T G T GA T G GC T TG T
SEO ID NO:	Genotype		
30-33	(IV/2b)	245	CGGCCTTGTATGTGGGaGACgTgTGCGGGGCCGTGATGATcGtGTCGCAGGCTtTCATAaT
34	(2c)	245	CTGCCCTTTATGTGGGGGACGTGTGTGGCGCGCTGATGCTGGCCGCTCAGGTCGTCGT
	(III/2a)	245	CcGCtCTtTACGTGGGGGAccTCTGCGGGGGGGTgATGCTCGCaGCcCAgATGTTCATtgT
26-29		245	CTGCGCTCTAcGTGGGLGATaTGTGTGGGGCCGTCTTCCTCGTGGGACAAGCCTTCACGTT
35-39	(V/3a)	243	CCGctATGTAcGTGGGGAtCTcTGCGGaTCtGTttCCTcgTcTCcCAGcTGTTCACctT
9-25	(II/1b)	245	CGGCCCTCTAcGTGGGGGACLTGTGCGGGTCTGTCTTCTCTGTCGGCCAaCTGTTCACCLT
1-8	(I/1a)	245	CGCCCTCTACGTGGGGGACTGTGGGGGGTCTTCTCTCTGTGGGCACATGTTCACCTGT
40	(4a)	245	CTGCCCTCTATGTTGGGGACCTCTGCGGAGGTGCCTTCCTGATGGGGCAGATGATCACTTT
42-43	(4C)	245	CtGCCTCTACgTTGGaGAtCTGTGCGGTGGtGCATTCTTGGTTGGcCAGATGTTcTCcTT
44	(4d)	245	CCGCCCTCTACATCGGAGACGTGTGTGGGGGGTGTGTTCTTGGTCGGTC
41	(4b)	245	CCGCCTTCTACATTGGAGATCTGTGGAGGCGTCTTCCTAGTGGGCCAGCTGTTCGACTT
45-50	(5a)	245	CCGCgcTATACGTCGGGGACGCGTGCGGGGCAgTGTTLLTGGTAGGCCAAATGTTCACCTA
51	(6a)	245	CATCCCTGTACATCGGGGACCTGTGTGGCTCTCTCTTTTTGGCGGGACAACTATTCACCTT
1-51	consensus		C TTA TGG GA TG GG T T CA T
SEO ID NO:	Genotype		
30-33	(IV/2b)	306	ATCGCCaGAACgCCACaACTTtACCCAaGAGTGCAACTGTTCCATCTACCAAGGTCatATC
34	(2c)	306	GTCGCCACACACCATACGTTTGTCCAGGAATGCAACTGTTCCATATACCCGGGCCGCATT
26-29	(III/2a)	306	CTCGCCGCaaCacCACTgGTTTGTGCAaGAaTGCAAtTGCTCcATcTACCCtGGtACCATC
35-39	(V/3a)	306	CAGACCECGTCGCCATCAAACGGTCCAGACCTGTAACTGCTCGCTGTACCCAGGCCAECTT
-	(II/1b)	306	CTCgCCtCGcCggcAtgaGACagtaCAGgAcTGcAAcTGcTCaaTCTATCCcGGcCacgTa
9-25		306	CTCtCCCAGgCgCcaCTGGACaACGCAaGaCTGcAAtTGTTCtATCTAtCCcGGCCAtATa
1-8	(I/la)	306	TOGGCCGCGTCGCCACTGGACCACGCAGGAGTGCAATTGTTCCATCTACACTGGCCATATC
40	(4a)	306	CCAGCCGCGACGCCACTGGACTACGCAGGACTGCAATTGTTCLATCTACGCAGGGCAtaTC
42-43	(4c)	306	CCAACCTCGCCGCCACTGGACCACCCAAGACTGCAATTGTTCCATCTACACAGGACATATC
44	(4d)	306	CCAACCTCGCCGCACTGGACCACCCAGGATTGCAACTGCTCCATCTATCCTGGTCACGTC
41	(4b)	306	CCGACCGCGCCGGCAC TGGACCACCAGGATTGGACTGCTGCATTTTTTTTTT
45-50	(5a)	306	TAGGCCTCGCCAGCAEACEACGGTGCAAGACTGCTACAGTTTACAGEGGCCAEATC TCAGCCCCGCCGTCATTGGACTGCAAGACTGCAACTGCTCCATCTATACAGGCCACGTC
51	(6a)	306	
1-51	consensus		CC C CA TG AA TG TC T TA GG T
SEO ID NO:	<u>Genotype</u>		
30-33	(IV/2b)	367	ACCGGCCACCGCATGGCATGGGACATGATGCTAAACTGGTCACCAACTCTLACCATGATCC
34	(2c)	367	ACGGGACACCGCATGGCTTGGGATATGATGATGAACTGGTCGCCCACTACCACCATGCTCC
26-29	(III/2a)	367	ACEGGRCACCGTATGGCATGGGACATGATGATGAACTGGTCGCCCACGGCCACCATGATCC
35-39	(V/3a)	267	TCBCCBCBTCGABTGGCTTGGGBTATGATGATGATTGGTCCCCCGCLGTGGGTATGGTGG
9-25	(II/1b)	367	tcaggtcaccgcatggcttgggatatgatgatgaactggtcacctaCagcagccctaGtgg
1-8	(I/la)	367	ACGGGtCAcCGcATGGCATGGGATATGATGATGAACTGGTCCCCLACgaCgGCgcTGGTag
40	(4a)	367	ACCEGCCACAGGATGGCGTGGGACATGATGAACTGGAGCCCTACCACCACTCTGCTCC
42-43	(4c)	367	ACGGGCCACAGGATGGCATGGGACATGATGATGAACTGGAGTCCCACAACCACCACGGTEC
•	(4d)	367	hcagacacagaatggcttgggacatgatgaattgagagccccactgcgacgctggtcc
44	1 1	301	TCGGGCCACAGGATGGCCTGGGACATGATGATGAACTGGAGCCCTACCAGCGCGCTGATTA
41	(4b)	30/	ACcGGCCACCGgATGGCaTGGGACATGATGATGAATTGGTCACCtaCgACaGCcTTGgTGA
45-50	(5a)	36/	ACCGCCACAGGATGGCTTGGGACATGATGATGATGTCACCCACAACCACTCTGGTCC
51	(6a)	367	C GG CA G ATGGC TGGGA ATGATG T AA TGG CC C T T
1-51	consensus		C GG CW G WIGGE 1999W WIGHTS I WW 199

#### FIGURE 1H

	SEO ID	NO: Genotype																					
	30-33	(IV/2b)	428	Tc	GCC.	TAt(	<b>GCcG</b>	CtCG	TG	Tt	CCIG	AgC	TAGt	:CCT	tgA	aGTt	:GTC	TTC	:GGc	:GG	CCA:	TG	GGG
	34	(2c)	428	TG	3CG	TAC	rrgg	TGCG	CA	TC	CCGG	AAG	TCAT	CIT	GGA:	TATI	GII	'ACA	GGZ	IGG:	TCA	TG	3GG
	26-29	(III/2a)	428	TG	3CG	TAC	GCGA	TGCG	CG	TT	CCCG	AGG	TCA7	Car	AGA	CATC	aTt	aGC	:GGg	,GC	tCA	:TGC	3GG
ř	35-39	(V/3a)	428	Tg	3CG(	CAC	TCC	TGCG	tt	TG	CCC	AGA	CCti	GII	CGA	CATA	a.Ta	GCC	:GGG	GC	CCA	TG	3GG
	9-25	(II/1b)	428	Ta?	rcg	CAgi	TaC	TCCG	ga	TC	CCaC	AAG	CTg1	<b>'CgT</b>	GGA	caTG	GTg	rgCg	GGg	rGC1	CCA	TG	3GG
	1-8	(I/1a)	428	Tac	3Ct(	CAĞ	TGC	TCcG	Ga	TC	CgC	'AaG	CCa7	CTT	GGA	CATG	ATC	GCI	GGt	:GC	CCA	TG	3GG
•	40	(4a)	428	TCC	3CC	CAG	AT'CA'	TGAG	GG	TC	CCCA	CAG	CCTI	TCI	CGA	CATG	GTI	GCC	GGJ	<b>I</b> GG	CCA	TGC	<b>G</b> G
	42-43	(4c)	428	TC	GCC(	CAG	TCA'	TGAG	GA	TC	CIA	GCA	CIC	GGT	aGA	<b>LCTA</b>	CTC	:gCI	GG	<b>I</b> GG	GCA(	TG	3GG
	44	(4d)	428	TC	3CC(	CAA	TTA	TGAG	GA	TC	CAG	GCG	CCAI	GGT	CGA	CCTG	CTI	'GCA	GGC	XGG(	CCA	TGC	3GG
	41	(4b)	428	TG	CT	CAG	ATCT	TACG	GΑ	TC	CCCI	CTA:	TCC1	ragg	TGA	CITC	CIC	'ACC	GGG	GG	TCA	TG(	3GG
	45-50	(5a)	428	TG	300	CAgt	TGC	TACG	GA	Tt(	CCC	'AgG'	TGG7	CAT	<b>EGA</b>	CATC	ATt	:GCC	GGG	:Gg(	CCA	TGC	3GG
	51	(6a)	428	TA	CI	agēj	ATCT	TGAG	GG	TA	CIG	AGA:	TTIC	TGC	GAG	IGIG	ATA	TII	GGI	GG	CCA!	TG	3GG
																	_						
	1-51	consensus		T	C			G		T	CC					T	T		GG	G	CA	TGG	<b>i</b> GG
	SEO ID	NO: Genotype						_															
	30-33	(IV/2b)	489	cG	GG	IGT.	MGG	CITG	GC	CT	TII	CIC	CATC	CAg	GGA	GCGI	GGG	CCA	Aac	TC	ATE	icc	TC
	34	(2c)	489	TG	CAA'	IGT:	rtgg	CCTC	GC	TT	CII	CIC	CATC	CAG	GGA'	rcgi	GGG	CGA	AGG	TC	ATC	117	TC
	26-29	(III/2a)	489	CG	Ca!	IGT:	rcGG	CtTa	GC	CI	CII	CIC	TATO	CAG	GGA	GCGI	GGG	CGA	AaG	TC	FIX	TC	TC
	35-39	(V/3a)	489	CA	rct:	TGG(	CgGG	CCTA	GC	CL	\TTA	CTC	CATO	CAg	GGC	AACI	GGG	CCA	AGG	TC	CI	TCE	TC
	9-25	(II/1b)	489	ag?	rcc.	TgG(	CGGG	CCTt	GC	CI	CIA	tTC(	CATO	Gtg	GGg	AACI	GGG	CEA	AGG	TE	tTg/	TTC	Tg
	1-8	(I/la)	489	AG.	rcc.	Tag	CGGG	CATA	GC	GI	ATTI	CIC	CATC	GtG	GGg)	AACI	GGG	CGA	AGG	TC	crgo	Tac	irg
	40	(4a)	489	CG	rcc	TCG	CGGG	CIIG	GC	GI	CII	CAG	CATC	CAA	GGC	AATI	GGG	CCA	AGG	TA	FICU	.TG0	FTC
	42-43	(4c)	489	cg?	rcc	rrg	rtgg	GtTG	GC	gT	ACTI	CaG	CATC	CAA	GCT	AATI	GGG	CCA	AaG	TC	ATC	760	310
	44	(4d)	489	CA	T.C.	IGG:	rrgg	CATA	GC	:GT2	CLI	CAG	CATC	CAA	GCIZ	AATT	GGG	CCA	AGG	1117	HICK	1160	71.0
	41	(4b)	489	AG.	rrc	TTG	TGG	TCTA	GC	TI.	CII	CAG	CATC	CAG	AGT/	AACI	<b>GGG</b>	CGA	AGG	TU	ATT CC	166	TC
	45-50	(5a)	489	GG:	CT	IGT:	rcGC	CGcc	GC	AT.	ACTE	CGC	GIC	GCG	GCE	AACI	700	TINA	220	TE	argu	100	olai.
	51	(6a)	489	GA:	rac	TAC:	rage	CGTT	GC	CL	CTI	TGG	CATE	iGCT.	تاتاتا	AAC I	GGC	TAA	MAU	111	LIGU	CIC	711
					r '	Г	G			T	т					т	GG	Δ	A G	т			T
	1-51	consensus		•		•	G		30	•	•						-	-		_			-
	SEO ID	NO: Genotype																					
	30-33	(IV/2b)	550	CTY	CT.	ter	IGTa	GCAG	GA	GT	GAt	GCA.											
	34	(2c)						GCTG															
	26-29	(III/2a)						GCTG															
	35-39	(V/3a)						TCAG															
	9-25	(II/1b)	550	aT	SCT.	ACT	TIN	GCcG	Gć	GT1	GAC	:GGq											
	1-8	(I/1a)	550	CI	SET	GCT	TIT	gCCG	GC	GT	GAt	:GCĞ											
	40	(4a)	550	CI	T	CCT	TIT	<u> GCTG</u>	ĠĠ	GT	AGAC	:GCC											
	42-43	(4c)						GCTG															
	44	(4d)	550	CIY	311	TCT	TIT	GCTG	GA	GT	CGAC	GCT											
	41	(4b)						GCCG															
	45-50	(5a)						GCGG															
	51	(6a)	550	CI	TI	CCT	ATTT	GCAG	GG	GT.	KADI	GCA											
		.,•			•																		
	1-51	consensus		T	T	T		CG	G	GT	GA	G											

## FIGURE 2A

	SEO ID NO:	<u>Isolate</u> S14	1 YOVRNSTGLYHVTNDCPNSSIVYEtADAILHaPGCVPCVREGNtSRCWVAMTPTVATRDGK
	52	DK7	1 YOVRNSTGLYHVTNDCPNSSIVYEAADAILHTPGCVPCVREGNVSRCWVAMTPTVATRDGK
	59	US11	1 YOVRNSTGLYHVTNDCPNSSIVYEAADAILHTPGCVPCVREGNASRCWVAMTPTVATRDGK
	55	DR4	1 HÓVRNSTGLÝHVINDCPNSSIVYBAADAILHTÞGCVÞCVREGNESRCWVAVTÞTVATRÓGK
	54	DR1	1 HOVRNSTGLÝHVINDCPNSSIVÝBAADAILHAPGCVPCVREGNASRCWVAVIPÍVATROGK 
	53	DK9	1 YOVRNSSGLYHVINDCPNSSIVYEAADAILHSPGCVPCVREGNASKCWVAVAPTVAIRDGK
	58	SW1	1 YQVRNSSGLYHVINDCPNSSIVYETADAILHSPGCVPCVREdgApKCWVAVAPTVATRDGK
	57	<b>S18</b>	
	52-59	consensus	yQVRNStGLYHVTNDCPNSSIVYEaADaILH-PGCVPCVRBgnasrCWVavtPTVATRDGK
	SEO ID NO:	<u>Isolate</u>	
	56	S14	62 LPatQLRRyIDLLVGSATLCSALYVGDLCGSVFLVGQLFTFSPRRlWTTQdCNCSIYPGHI
	52	DK7	62 LPTaOLRRHIDLLVGSATLCSALYVGDLCGSVFLVGOLFTFSPRRHWITGGCNCSIYPGHI
	59	US11	62 LPTTQLRRHIDLLVGSATLCSALYVGDLCGSVFLVGQLFTFSPRRHWTTQGCNCSIYPGHI
	55	DR4	62 LPTTQLRRHIDLLVGSATLCSALYVGDLCGSVFLVGQLFTFSPRhHWTTQDCNCSIYPGHI
	54	DR1	62 LPTTOLRRHIDLINGSATLCSALYVGDLCGSVFLVGOLFTFSPRRHWTTODCNCSIYPGHI
	53	DK9	62 LPATOLRRHIDLLVGSATLCSALYVGDLCGSVFLVGOLFTFSPRRHWTTODCNCSIYPGHI
	58	SW1	62 LPATOLRRHIDLLVGSATLCSALYVGDLCGSVFLVSQLFTFSPRRHWTTQDCNCSIYPGHI
	57	S18	
	52-59	consensus	LP-cQLRRhIDLLVGSATLCSALYVGDLCGSVFLVgQLFTfSPRrhWTTQdCNCSIYPGHI
	SEO ID NO:	<u>Isolate</u>	
	56	S14	123 TGHRMAWDMMMNWSPTTALVVAQLLRIPQAILDMIAGAHWGVLAGIAYFSMVGNWAKVLVV
	52	DK7	123 TGHRMAWDMMMNWSPTTALVVAOLLRIPOAILDMIAGAHWGVLAGIAYPSMVGNWAKVLVV
	59	US11	123 TGHRMAWDMYNNWSPTAALVVAOLLRIPOAILDMIAGAHWGVLAGIAYFSMVGNWAKVLVV 
	55	DR4	123 TGHRMAWDMMMNWSPTTALVVAQLLRIPQAILDMIAGAHWGVLAGIAYFSMVGNWAKVLVV
	54	DR1	123 TGHRMAWDMMNWSPTTALVMAQLLRIPQAILDMIAGAHWGVLAGIAYFSMVGNWAKVVVV
	53	DK9	123 TGHRMAWDMMMNWSPTAALVMAOLLRIPOAILDMIAGAHWGVLAGIAYFSMVGNWAKVVVV
	58	SW1	
	57	\$18	123 TGHRMAWDMMMNWSPTTALVIAQLLRvPQAVLDMIAGAHWGVLAGIAYFSMAGNWAKVLlV
•	52-59	consensus	TGHRMAWDMMNWSPTtalvvaQllripQaildMlagaHwgVlaglayfsmvgnwaKVlvV

## FIGURE 2A

SEO ID NO:	<u> Isolate</u>	
56	S14	184 LLLFAGVDA
		[ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [ [
52	DK7	184 LLLFAGVDA
		1111111
5 <del>9</del>	<b>US11</b>	184 LLLFAGVDA
		11111111
55	DR4	184 LLLFAGVDA
		111111111
54	DR1	184 LILFAGVDA
		1111 [111
53	DK9	184 LLLFtGVDA
		1111 1111
58	SW1	184 LLLFBGVDA
		1111 1111
57	<b>\$18</b>	184 LLLFaGVDA
52-59	consensus	LLLFaGVDA

SEO ID NO:	Isolate		
75	T10	1 YEVRNVSGmYHVTNDCSNSSIVfEAaDlIMHTPGCVPCVREgNsSRCWVALTFTLA	ARNES
••			111 1
62	DK1	1 YEVRNÝSGVÝHÝTNÍCSNSSÍVYBAVÍVÍMHTPGCVPCVRENNÍSRCWVALTPTLA	ARNAS
<b>02</b>			11111
64	HK4	1 hEVHNVSG1YHVTNDCSNSSIVYRAADMIMHTPGCVPCVRENNSSRCWVALTPTLA	ARNAS
••			11111
76	US6	1 YEVRNÝSÉMÝHÝTNÍCSNSSÍVÝBAADMÍMHTPGCVPCVRENNSSRCWVALTPTLA	ARNAS
			11111
68	IND8	1 YEVRNYSGVYHYTNDCSNSSTVYRAADMIMHTPGCVPCVREGNESSCWVALTPTLA	ARNAS
00			11111
67	IND5	1 YEVRNÝSGVÝHÝTNÍCSNSSÍVÝRAADMIMHTPGCVPCVREGNSSRCWVALTPTLA	ARNAS
<b>.</b>	2		
73	SW2	1 YEVRNVSGVYHVINDCSNSSIVYETADMIMHTPGCVPCVREaNSSRCWVALTPTLA	ARNES
13	5112		111 1
63	HK3	1 YEVRNVSGIYHVTNDCSNSSVVYETADMIMHTPGCVPCVRENNSSRCWVALTPTLA	ARNVS
63	1110		11111
66	нк8	1 YEVRNVSGIYHVTNDCSNSSIVYETADMIMHTPGCmPCVRBNNSSRCWVALTPTLA	ARNVS
90	IIVo		1111
	Д3	1 YEVRNVSGVYGVTNDCSNSSIVYETADMIMHTPGCVPCVRBdNSSRCWVALTPTLA	ARNES
61	בע		
	Т3	1 YEVRNVSGVYyVTNDCSNSSIVYETADMIMHTPGCVPCVRE#NSSRCWVALTPTLA	ARNAS
74	13	1 YEVRNVSGVYYVINDCSNSSIVYETADMIEHTPGCVPCVRBBNSSRCWVALIFFILM	11111
	HKS	1 YEVRNVSGVYHVINDCSN1SIVYETtDMIMHTPGCVPCVRENNSSRCWVALaPTLA	ARNAS
65	HV2		
	S45	1 YEVRNVSGaYHVTNDCSNSSIVYKAVDVIIHTPGCVPCVRENNSSRCWVALTPTLA	ARNSS
71	242		11111
=0	SA10	1 YEVRNVSGmYHVINDCSNSSIVYEAADMIMHTPGCVPCVRENNSSRCWVALTPTLA	ARNSS
72	SALU		11111
<b>5</b> 0	22.0	1 YEVRNVSGVYHVTNDCSNSSIVYRAADMIMHTPGCVPCVRENNSSRCWVALTPTLA	ARNSS
69	P10		111
		1 VEVPNVSGVYHVTNDCSNSSIVYRtADMIMHTPGCVPCVREdNSSRCWVALTPTLA	ARNgn
60	. <b>D1</b>	1 YEVRNVSGVYHVTNDCSNSSIVYKŁADMIMHTPGCVPCVREGNSSRCWVALTPTLA	
=0	20	1 YEVRNVSGaYHVTNDCSNSSIVYEAADvIMHTPGCVPCVqEgNSSqCWVALTPTLA	APNat
70	<b>S9</b>	T IDAMAGGENATURCHIGGE ATOMENATURE CALCAGRANDO CHANNET INC	
co =c		yEV:nVSGvYhVTNDCSNsSiVyEaaDmImHTPGCvPCVrEnNsSrCWVALtPTLA	ARNac
60-76	consensus	APATHAGGATHATHINGSHPGTAANGGATHINGTEGCAECATHINGGGTCHANNCETHAG	

SEO ID NO	: Isolate		
75	T10	62	vPTTTIRRHVDLLVGAAAFCSAMYVGDLCGSVFLVSQLFTFSPRRHET1QDCNCSIYPGH1
			TPTTTTRRHVDLLVGAAAFCSAMYVGDLCGSVFLVSOLFTFSPRRHETaODCNCSIYPGHV
62	DK1	62	IPTTTIRRHVDLLVGAAAFCSAMYVGDLCGSVFLVSQLFTFSPRRHETaQDCNCSIYFGHV
•	HK4	62	TPTTTTPPHVDLLVGAAAFCSAMYVGDLCGSVFLVSOLFTFSPRRHETVODCNCSIYPGHV
64	III.4	94	
76	US6	62	VPTTTIRRHVDLLVGAALPCSAMYVGDLCGSVFLiSQLFTFSPRQHETVQDCNCSIYPGHV
, ,,	000	-	
68	IND8	62	VPTTTTRRHVDLLVGAAAFCSAMYVGDLCGSVFLVSQLFTFSPRRHETVQDCNCSIYPGHV
67	IND5	62	VETTTIRhHVDLLVGAAAFCSAMYVGDLCGSVFLVSQLFTFSPRRHETVQDCNCSIYPGHV
73	SW2	62	VPTTTTRRHVDLLVGAAAFCSVMYVGDLCGSVFLVSQLFTFSPRRHKTVQDCNCSTYPGHV
63	HK3	62	
	HK8	62	VPTTTTPPHVDLLVGAAAFCSAMYVGDLCGSVFLVSOLFTFSPRRHETVODCNCSIYPGHV
66	na	6.4	TITLE TO THE TENED OF T
61	D3	62	UPTTTT DDHVIDT.LVGAAAFCSAMYVGDLCGSVFLVSOLFTFSPRRHETVOeCNCSTYPGHV
97	נע	62	
74	Т3	62	VPTKTIRRHVDLLVGAAAFCSAMYVGDLCGSVFLVSQLFTFSPRRHETVQDCNCSIYPGHV
•			
65	HK5	62	VPTTaIRRHVDLLVGAAAFCSAMYVGDLCGSVFLVSQLFTFSPRRHETVQDCNCSIYPGHV
71	S45	62	VPTTTTRRHVDLLVGAAAFCSAMYVGDLCGSVFLVSQLFTFSPRRHETVQDCNCSIYPGHV
			VIDITET TOPHVDLLVGAAAFCSAMYVGDLCGSVFLVSOLFTFSPRRVETVODCNCSIYPGTV
72	SA10	62	VPTTTIRRHVDLLVGAAAFCSAMYVGDLCGSVFLVSQLFTFSPRRYETVQDCNCSIYPGTV
69	P10	62	THE TOTAL TO
65	PIO	02	111111111111111111111111111111111111111
60	D1	62	VPTTAIRRHVDLLVGAAAFCSAMYVGDLCGSVFLISQLFT1SPRRHETVQeCNCSIYPGHV
70		-	
70	S9	62	VPTTtIRRHVDLLVGAAvFCSAMYVGDLCGSVFLISQLFTiSPRRHETVQnCNCSIYPGHV
60-76	consensus		$\verb"vpTttlr" HVDLLVGAAaFCSaMYVGDLCGSVflvSQLFTfSPRrheTvQdCNCSiYPGhv"$

SEO ID NO	: <u>Isolate</u>		
75	T10	123 SGHRMAWDMMNWSPTTALVVSQLLRIPQAVmDMVtGAHWGVLAG	LAYYSMAGNWAKVLIV
62	DK1	123 SGHRMAWDMMNWSPTTALVISQLLRIPQAVvDMVAGAHWGVLAG	LAYYSMAGNWAKVLIV
64	HK4	123 SGHRMAWDMMMNWSPTAALVVSQLLRLPQAVMDMVAGAHWGVLAG	LAYYSMVGNWAKVLIV
76	US6	123 SGHRMAWDMMMNWSPTAALVVSQLLRIPQAVMDMVAGAHWGVLAGI	AYYSMVGNWAKVLIV
68	IND8	123 SGHRMAWDMMMWSPTAALVVSQLLRIPQAVVDMVAGAHWGILAG	AYYSMVGNWAKVLIV
67	INDS	123 SGHRMAWDMMNWSPTAALVVSOLLRIPOAVVDMVAGAHWGILAGI	AYYSMVGNWAKVLIV
•			
73	SW2	123 SGHRMAWDMMNWSPTAALVVSQLLRIPQAVVDMVAGAHWGVLAGI	AYYSMVGNWAKVLIV
ഒ	HK3	123 SGHRMAWDMMNWSPTAALVVSOLLRIPOAVVDMVAGAHWGVLAGI	AYYSMUGNWAKULIV
•••			
66	HKB	123 SGHRMAWDMMNWSPTtALVVSOLLRIPOAiVDMVAGAHWGVLAGI	AYYSMVGNWAKVI.TV
00	1110		
61	D3	123 TGHRMAWDMMNWSPTaALVVSOLLRIPOAVVDMVAGAHWGVLAGI	.TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT
61	23	111111111111111111111111111111111111111	
74	Т3	123 TGHRMAWDMMNWSPITALVVSOLLRIPOAVVDMVAGAHWGVLAGI	AVVENUENWANT.TI
/4	13	123 1GARMADIMENTASETTABAASQUIRTEGAAADIMAAAITASAMAA	IIIIIIIIIIIIII
65	HKS	123 TGHRMAWDMMMWSPTTALVVSOLLRIPOAVVDMVAGAHWGVLAGI	AYYSMVGNWAKVLIV
63	- An	11111111111111111111111111111111111111	[
71	S45	123 TGHRMAWDMMMNWSPTaALVVSOLLRIPOAVVDMVAGAHWGVLAGI	AVVENUIZNWA KUIT.TII
12	343	123 IGRAMANDATAN SPIRADOV SOMECTE DA VIDA SALAGO MASA	11111111111111
72	SA10	123 TGHRMAWDMMNWSPTTALVVSOLLRIPOAIVDMVAGAHWGVLAGI	AVVSMAZAWAYATATA
12	SALU	123 IGREMADIMENTASE CADA ASSUME LA SEL ASSUMBATION ASSUMBLE SEL ASSUMB	11111111111111
69	P10	123 gGHRMAWDMMNWSPTaALVVSOLLRIPOAIlDvVAGAHWGVLAGI	.
69	PIU	11111111111111111111111111111111111111	11111111111111
60	D1	123 TGHRMAWDMMNWSPTTALVVSOLLRIPOAVMDMVAGAHWGVLAGI	AYYSMVGNWAKVLTV
90	DI	1   1   1   1   1   1   1   1   1   1	1111111111111
70	S9	123 TGHRMAWDMMNWSPTTALVVSQLLRIPQAVMDMVAGAHWGVLAGI	AVVENUENWANTETT
70	27	TV2 TOUGHWINITHMUSETTWIN ASSURETS OWALING AND WING A THOSE	MI TOTA GRANICATITA
60-76	5000000000	sghrmawdmmmnwsptaalvvsqllripqavvdmvagahwgvlagli	VVCM-CNWNYCTT.TT
DU-10	consensus	POUNTHUDITATION LOND A SOUTH TO A SOUTH TO SOUTH THE SOU	T TOMAGNAMWEATTA

Isolate		
T10	184	mLLFAGVDG
DK1	184	1LLFAGVDG
HK4	184	mLLFAGVDG
US6	184	
IND8	184	MILLFAGVDG
INDS	184	MLLFAGVDG
SW2	184	MLLFAGVDG
		111111111
		111111111
		111111111
		MLLFAGVDG
T3	184	1LLFAGVDG
HKS	184	MLLFAGVOG
\$45	184	MLLFAGVDG
SA10	184	MILFAGVOG
P10	184	MLLFAGVDG
<b>D1</b>	184	MLLFAGVDG
S9	184	MLLFAGVDG
consensus		mLLFAGVDG
	DK1 HK4 US6 IND8 IND5 SW2 HK3 HK8 D3 T3 HK5 S45 SA10 P10 D1 S9	T10 184  DK1 184  HK4 184  US6 184  IND8 184  INDS 184  SW2 184  HK3 184  HK8 184  D3 184  T3 184  HK5 184  SA10 184  P10 184  D1 184  S9 184

## FIGURE 2C

	SEO ID NO:	<u>Isolate</u>	_	
	77	T2	. 1	AQVrnTsrgYMVTNDCSNeSITWQIQAAVLHVPGCiPCErlGnTSRCWIPVtPNVAVRQPG
•	78	T4	1	AQVKNTtmSYMVTNDCSNDSITWOLQAAVLHVPGCVPCRktGNTSRCWIPVSPNVAVRQPG
	79	<b>T9</b>	1	AeVKNTSTSYMVTNDCSNDSITWQLQAAVLHVPGCVPCErVGNaSRCWIPVSPNVAVQRPG
•	80	<b>US10</b>	1	VQVKNTSTSYMVTNDCSNDSITWQLeAAVLHVPGCVPCEKVGNtSRCWIPVSPNVAVQRPG
	77-80	consensus		aqvkntstsymvtndcsndsitwqlqaavlhvpgcvpcb-vgntsrcwipvspnvavpg
				•
	SEO ID NO:	<u> Isolate</u>		
	77	T2	62	ALTOGLETHIDMVVMSATLCSALYVGDLCGGVMLAAQMFIVSP::HWFVQeCNCSIYPGTI
	78	T4	62	ALTOGLRTHIDMVVMSATLCSALYVGDLCGGVMLAAQMFIVSPQHHWFVQdCNCSIYPGTI
	79	Т9	62	ALTQGLRTHIDMVVMSATLCSALYVGDLCGGVMLAAQMFIiSPQHHWFVQECNCSIYPGTI
	80	US10	62	ALTOGLETHIDMVVMSATLCSALYVGDfCGGmMLAAQMFIvSPrHHsFVQECNCSIYPGTI
				•
	77-80	consensus		ALTQGLRTHIDMVVMSATLCSALYVGDlCGGvMLAAQMFIvSP-hHwFVQeCNCSIYPGTI
	SEO ID NO:	<u>Isolate</u>		
	SEO ID NO: 77	<u>Isolate</u> T2	123	TGHRMAWDMMMNWSPTATMILAYAMRVPEVIiDIigGAHWGVMFGLAYFSMQGAWAKViVI
				TGHRMAWDMMNWSPTATMILAYAMRVPEVIIDIIgGAHWGVMFGLAYFSMQGAWAKVIVI
	77	<b>T</b> 2	123	
	77 78 79	T2 T4 T9	123 123	TGHRMAWDMMNWSPTATMILAYAMRVPEVILDIVSGAHWGVMFGLAYPSMOGAWAKUVVI
	77 78 79 80	T2 T4 T9 US10	123 123	TGHRMAWDMMMNWSPTATMILAYAMRVPEVIlDIvSGAHWGVMFGLAYPSMQGAWAKVVVI TGHRMAWDMMNWSPTATMILAYAMRVPEVILDIISGAHWGVMFGLAYPSMQGAWAKVVVI TGHRMAWDMMNWSPTATMILAYAMRVPEVILDIISGAHWGVMFGLAYPSMQGAWAKVVVI TGHRMAWDMMNWSPTATTIILAYVMRVPEVILDIISGAHWGVFGLAYFSMQGAWAKVVVI
	77 78 79	T2 T4 T9	123 123	TGHRMAWDMMNWSPTATMILAYAMRVPEVILDIVSGAHWGVMFGLAYPSMOGAWAKUVVI
	77 78 79 80	T2 T4 T9 US10 Consensus	123 123	TGHRMAWDMMMNWSPTATMILAYAMRVPEVIlDIvSGAHWGVMFGLAYPSMQGAWAKVVVI TGHRMAWDMMNWSPTATMILAYAMRVPEVILDIISGAHWGVMFGLAYPSMQGAWAKVVVI TGHRMAWDMMNWSPTATMILAYAMRVPEVILDIISGAHWGVMFGLAYPSMQGAWAKVVVI TGHRMAWDMMNWSPTATTIILAYVMRVPEVILDIISGAHWGVFGLAYFSMQGAWAKVVVI
	77 78 79 80 77-80	T2 T4 T9 US10	123 123 123	TGHRMAWDMMMNWSPTATMILAYAMRVPEVIlDIvSGAHWGVMFGLAYPSMQGAWAKVVVI TGHRMAWDMMNWSPTATMILAYAMRVPEVILDIISGAHWGVMFGLAYPSMQGAWAKVVVI TGHRMAWDMMNWSPTATMILAYAMRVPEVILDIISGAHWGVMFGLAYPSMQGAWAKVVVI TGHRMAWDMMNWSPTATTIILAYVMRVPEVILDIISGAHWGVFGLAYFSMQGAWAKVVVI
	77 78 79 80 77-80 SEO ID NO:	T2 T4 T9 US10 Consensus Isolate	123 123 123	TGHRMAWDMMMNWSPTATMILAYAMRVPEVIIDIVSGAHWGVMFGLAYFSMQGAWAKVVVI  TGHRMAWDMMMNWSPTtTMILAYAMRVPEVIIDIISGAHWGVMFGLAYFSMQGAWAKVVVI  TGHRMAWDMMMNWSPTATTIILAYAMRVPEVIIDIISGAHWGVMFGLAYFSMQGAWAKVVVI  TGHRMAWDMMMNWSPTATTIILAYAMRVPEVIIDIISGAHWGVMFGLAYFSMQGAWAKVVVI  TGHRMAWDMMMNWSPTATMILAYAMRVPEVIIDIISGAHWGVMFGLAYFSMQGAWAKVVVI
	77 78 79 80 77-80 SEO ID NO:	T2 T4 T9 US10 Consensus Isolate T2	123 123 123 123	TGHRMAWDMMMNWSPTATMILAYAMRVPEVIIDIVSGAHWGVMFGLAYFSMQGAWAKUVVI  TGHRMAWDMMMNWSPTCTMILAYAMRVPEVIIDIISGAHWGVMFGLAYFSMQGAWAKUVVI  TGHRMAWDMMMNWSPTCTMILAYAMRVPEVIIDIISGAHWGVMFGLAYFSMQGAWAKVVVI  TGHRMAWDMMMNWSPTCTMILAYAMRVPEVIIDIISGAHWGVNFGLAYFSMQGAWAKVVVI  TGHRMAWDMMMNWSPTCTMILAYAMRVPEVIIDIISGAHWGVMFGLAYFSMQGAWAKVVVI  LLLAAGVDA
	77 78 79 80 77-80 SEO ID NO: 77	T2 T4 T9 US10 Consensus Isolate T2 T4	123 123 123 184 184 184	TGHRMAWDMMMNWSPTATMILAYAMRVPEVIlDIvSGAHWGVMFGLAYFSMQGAWAKVVVI  TGHRMAWDMMNWSPTTMILAYAMRVPEVIIDIISGAHWGVMFGLAYFSMQGAWAKVVVI  TGHRMAWDMMNWSPTATTIILAYAMRVPEVIIDIISGAHWGVIFGLAYFSMQGAWAKVVVI  TGHRMAWDMMMNWSPTATTIILAYAMRVPEVIIDIISGAHWGVMFGLAYFSMQGAWAKVVVI  LLLAAGVDA  LLLAAGVDA  LLLAAGVDA  LLLAAGVDA
	77 78 79 80 77-80 SEO ID NO: 77 78 79	T2 T4 T9 US10 Consensus Isolate T2 T4 T9	123 123 123 184 184 184	TGHRMAWDMMMNWSPTATMILAYAMRVPEVIlDIvSGAHWGVMFGLAYPSMOGAWAKVVVI  TGHRMAWDMMMNWSPTCTMILAYAMRVPEVIIDIISGAHWGVMFGLAYPSMOGAWAKVVVI  TGHRMAWDMMMNWSPTCTMILAYAMRVPEVIIDIISGAHWGVIFGLAYFSMQGAWAKVVVI  TGHRMAWDMMMNWSPTCTMILAYAMRVPEVIIDIISGAHWGVIFGLAYFSMQGAWAKVVVI  LLLAAGVDA  LLLAAGVDA  LLLAAGVDA  LLLAAGVDA  LLLAAGVDA  LLLAAGVDA  LLLAAGVDA  LLLAAGVDA  LLLAAGVDA

37./47

# FIGURE 2D

	8EO ID NO: 82 83 84 81	Isolate DK11 SW3 T8 DK8	1	VEVRNtSSSYYATNDCSNnSITWQLTNAVLHLPGCVPCENDNGTLHCWIQVTPNVAVKHRG
2	82 NO:	Isolate DK11		ALTHNIRAHIDMIVMAATVCSALYVGDVCGAVMIVSQAFIVSPEHHLFTQECNCSIYQGLI
	83	SW3	62	ALTHNLRAHVDMIVMAATVCSALYVGDmCGAVMIVSQAFIISPERHNFIQECNCSIYQGTI
	84	T8	62	ALTHNIRTHVDVIVMAATVCSALYVGDVCGAVMIASQAFIISPERHNFTQECNCSIYQGHI
	81	DK8	62	ALTHNIRTHVDVIVMAATVCSALYVGDVCGAVMIvSQALIISPERHNFTQECNCSIYQGHI
8	11-84	consensus		ALTHNLR-HvD-IVMAATVCSALYVGDvCGAVMIvSQAfIiSPErHnFTQECNCSIYQGhI
<u>\$</u>	82 83	Isolate DK11 SW3		TGHRMAWDMMLNWSPTLTMILAYAARVPELVLEVVFGGHWGVVFGLAYFSMQGAWAKVIAI
	84	Т8	123	TGHRMAWDMMINWSPTLTMILAYAARVPELVLEVVFGGHWGVVFGLAYFSMQGAWAKVIAI
	81	DK8	123	TGHRMAWDMMLNWSPTLTMILAYAARVPELaLqVVFGGHWGVVFGLAYFSMQGAWAKVIAI
8	1-84	consensus		TGHRMAWDMMLNWSPTLTMILAYAARVPELvLeVVFGGHWGVVFGLAYFSMQGAWAKVIAI
<u>s</u>	SEO ID NO:	<u>Isolate</u> DK11	184	LLLVAGVDA
	83	SW3	184	ILLVAGVDA
	84	<b>T</b> 8	184	LLLVAGVDA
	81	DKS	184	LLLVAGVDA
8	11-84	consensus		LILVAGVDA

## FIGURE 2E

SEO ID NO:	<u>Isolate</u> DK12	1 LEWRNVSGLYVLTNDCsNSSIVYEADDVILHTPGCVPCVQDGNTSTCWTSVTPTVAVRYVG
. 87	HK10	
88	S2	1 LEWRNTSGLYVLINDCSNSSIVYRADDVILHTPGCVPCVODGNTSTCWTPVTPTVAVRYVG
90	S54	1 LEWRNTSGLY:LINDCSNSSIVYEADDVILHIPGCVPCVDDGNTSTCWTPVTPTVAVRYVG
89	S52	1 LEWRNTSGLÝ-VLTNDCSNSSÍVÝRADDVÍLHTPGCVPCVQDGNTSmCWTPVTPTVÁVRÝVG
86-90	consensus	LEWRNtSGLY~LTNDCsNSSIVYEADDVILHTPGCVPCVQDGNTStCWTpVTPTVAVRYVG
SEO ID NO:	<u>Isolate</u> DK12	62 ATTASIRSHVDLLVGAATMCSALYVGD∀CGAVFLVGQAFTFRPRRHQTVQTCNCSLYPGHL
87	HK10	
88	S2	
90	S54	62 ATTASIRSHVDLLVGAATLCSALYVGDMCGAVFLVGQAFTFRPRRHQTVQTCNCSLYPGHL
89	S52	62 ATTASIRSHVDLLVGAATLCSALYVGDMCGAVFLVGQAFTFRPRRHQTVQTCNCSLYPGHV
86-90	consensus	ATTASIRSHVDLLVGAATmCSALYVGDmCGAVFLVGQAFTFRPRRHQTVQTCNCSLYPGH1
SEO ID NO:	<u>Isolate</u> DK12	123 SGHRMAWDMMNWSPAVGMVVAHVLRLPQTLFDIIAGAHWGIMAGLAYYSMQGNWAKVAII
.87	HK:1.0	
88	S2	123 SGHRMAWDMMNWSPAVGMVVAHVLRLPOTvFDIIAGAHWGILAGLAYYSMOGNWAKVAII
90	<b>\$54</b>	123 SGHRMAWDMMMWSPAVGMVVAHILRLPOTLFDILAGAHWGILAGLAYYSMOGNWAKVAII
89	\$52	123 SGHRMAWDMMMNWSPAVGMVVAHILRLPQTLFDILAGAHWGILAGLAYYSMQGNWAKVAIv
86-90	consensus	SGHRMAWDMMMNWSPAVGMVVAH~LRLPQT1FDIiAGAHWGI1AGLAYYSMQGNWAKVAIi
SEO ID NO:	<u>Isolate</u> DK12	184 MVMFSGVDA
87	HK10	 184 MVMFSGVDA
88	S2	 184 MVMFSGVDA 
90	S54	184 MIMFSGVDA
89	\$52	184 MIMFSGVDA
♥ 86-90	consensus	M√MFSGVDA

\$

## FIGURE 2F

SEO ID NO: 93	<u>Isolate</u> 27 <b>2</b> 6	_	VNYhNASGVYHITNDCPNSSImYEAEHHILHLPGCVPCVReGNQSRCWVALTPTVAAPYIG 
93-94 consen	sus (Z6)		VNY±NASGVYHVTNDCPNSSIVYRAEHqILHLPGC1PCVRvGNQSRCWVALTPTVAveYIG
SEO ID NO:	Isolate 27		APLESIRRHVDLMVGAATVCSALYIGDLCGGVFLVGOMPSFOPRRHWTTQDCNCSIYAGHV
94 93-94 consens	Z6 sus (Z6)	62	APLdSLRRHVDLMVGAATVCSALYvGDLCGGaFLVGQMFSFQPRRHWTTQDCNCSIYAGHI APLdSlrrhvDLMVGAATVCSALYvGDLCGGaFLVGQMFSFQPRRHWTTQDCNCSIYAGHi
SEO ID NO:	<u>Isolate</u> Z7	.123	TGHRMAWDMMNWSPTTTLvLAQVMRIPSTLVDLLTGGHWGiLiGVAYFCMQANWAKVILV
94	<b>Z</b> 6	123	TGHRMAWDMMNWSPTTTLllaQVMRIPSTLVDLLAGGHWGVLVGLAYPSMQANWAKVILV
93-94 consens	sus (26)		TGHRMAWDMMNNWSPTTTLllaQvMRiPSTLVDLLaGGHWGvLvGlaYFaMQANWAKVILV
SEO ID NO:	<u>Isolate</u> Z7	184	LFLYAGVDA
94	26	184	LFLFAGVDA
93-94 consens	sus (26)		LFLEAGVDA

## FIGURE 2G

SEO ID NO: 98  100  97  96  99  101  96-101	Isolate SA5 SA7 SA4 SA1 SA6 SA13 consensus	1 1 1 1	VPYRNASGVYHVINDCPNSSIVYEADNLILHAPGCVPCVKegNVSRCWVQITPTLSAPNLG  VPYRNASGVYHVINDCPNSSIVYEADNLILHAPGCVPCVRQnNVSRCWVQITPTLSAPNLG  VPYRNASGVYHVINDCPNSSIVYEADNLILHAPGCVPCVRQDNVSKCWVQITPTLSAPNLG  VPYRNASGVYHVINDCPNSSIVYEADNLILHAPGCVPCVRQDNVSRCWVQITPTLSAPNLG  VPYRNASGVYHVINDCPNSSIVYEADBLILHAPGCVPCVRQDNVSRCWVQITPTLSAPLG  VPYRNASGVYHVINDCPNSSIVYEADDLILHAPGCVPCVRDNVSRCWVhITPTLSAPSIG  VPYRNASGVYHVINDCPNSSIVYEADDLILHAPGCVPCVRQBNVSRCWVQITPTLSAPSIG  VPYRNASGVYHVINDCPNSSIVYEADDLILHAPGCVPCVRQBNVSRCWVQITPTLSAPSIG
SEO ID NO: 98  100 97 96 99 101 96-101	Isolate SA5 SA7 SA4 SA1 SA6 SA13	62 62 62 62	AVTAPLRRAVDYLAGGAALCSALYVGDACGAVFLVGQMFTYRPRQHTTVQDCNCSIYSGHI  AVTAPLRRAVDYLAGGAALCSALYVGDACGAVFLVGQMFBYRPRQHTTVQDCNCSIYSGHI  AVTAPLRRAVDYLAGGAALCSALYVGDACGAVFLVGQMFTYRPRQHTTVQDCNCSIYSGHI  AVTAPLRRAVDYLAGGAALCSALYVGDACGAVFLVGQMFTYRPRQHTTVQDCNCSIYSGHI  AVTAPLRRAVDYLAGGAALCSALYVGDACGAVFLVGQMFTYRPRQHTTVQDCNCSIYSGHI  AVTAPLRRAVDYLAGGAALCSALYVGDVCGALFLVGQMFTYRPRQHATVQDCNCSIYSGHI  AVTAPLRRAVDYLAGGAALCSALYVGDVCGALFLVGQMFTYRPRQHATVQDCNCSIYSGHI  AVTAPLRRAVDYLAGGAALCSALYVGDACGAVFLVGQMFTYBPRTHDVVQDCNCSIYSGHI  AVTAPLRRAVDYLAGGAALCSALYVGDACGAVFLVGQMFTYBPRTHDVVQDCNCSIYSGHI  AVTAPLRRAVDYLAGGAALCSALYVGDACGAVFLVGQMFTYBPRTHDVQDCNCSIYSGHI
SEO ID NO: 98 100 97 96 99 101 96-101	Isolate SA5 SA7 SA4 SA1 SA6 SA13	123 ° 123 ° 123 ° 123 ° 123 ° 123 ° 1	TGHRMAWDMMMNWSPTTALVMAQvLRIPQVVIDIIAGGHWGVLFAVAYFASAANWAKVVLV

## FIGURE 2G

	SEO ID NO:	<u>Isolate</u>		
	98	SA5	184	
				11111111
	100	SA7	184	LFLFAGVDA
				111111111
•	97	SA4	184	
				11111111
	96	SAL	184	LFLFAGVDg
_		-		
	99	SA6	184	LFLFAGVDA
				1111111111
	101	SA13	184	
	<del></del>			
	96-101	consensus		LPLFAGVDa

## FIGURE 2H

SEO ID NO 81-84 85 77-80 86-90 60-76 52-59 91 93-94 95 92 96-101	: Genotype (IV/2b) (2c) (III/2a) (V/3a) (II/1b) (I/1a) (4a) (4c) (4d) (4d) (5a)	1 VE 1 aq 1 LE 1 yE 1 yC 1 EH 1 VN 1 YN 1 VH 1 VF	VKDTGDSYI VKNTETEY WRNTSGLY: VRNSTGLY: VRNSSGLY! YRNASGVYI YRNASGVYI YRNASGVYI YRNASGVYI YRNASGVYI YRNASGVYI	MPTNDCS MVTNDCS VLTNDCS hVTNDCS HVTNDCP HITNDCP HVTNDCP HVTNDCP HVTNDCP HVTNDCP	VISEN VISEN VISEN VISEN VISEN VISEN VISEN VISEN	WQLEGA TWQLGAA JYEADDV JYEAADA JYEAADA JYEADHH JYETDYH JYETDYH JYETEHH JYEADAL	VLHTPGC VLHVPGC ILHTPGC ILHSPGC ILHLPGC ILHLPGC ILHLPGC ILHLPGC ILHLPGC ILHLPGC ILHLPGC	VPCERTA VPCEKVG VPCVPEN VPCVREG VPCVRTG VPCVRTG VPCVRTG VPCVRTG VPCVRTG	MVSRCWV INTSTCWI INTSTCWV INBSTCWV INTSRCWT INQSRCWV INKSTCWV INTSRCWV INTSRCWV	QVTPNVAVKHRO PVAPNLAISQPO PV6PNVAVqqPG pVTPTVAVRYVG ALtPTLAARNA6 avtPTVATRDGK PVTPTVAVAHPG ALTPTVAVAHPG SLTPTVAAQHLN PLTPTVAAPYPN qITPTLSAPNA6 AVTPTLAIPNAS	
102	(44)	1 41									•
52-102	consensus		Y	TNDC	N S		H PGC	PC	CW	P	
SEO ID NO: 81-84 85 77-80 86-90 60-76 52-59 91 93-94 95 92 96-101 102	Genotype (IV/2b) (2c) (III/2a) (V/3a) (II/1b) (I/1a) (4a) (4c) (4d) (4b) (5a) (6a)	62 AL 62 AT 62 VP 62 LP 62 AP 62 AP 62 AP 62 AP 62 AV	KGLRAHII CGLRTHII CASIRSHVI CEEIRHVI LESFRRHVI LGSIRRHVI LGSIRRHVI LESMRRHVI LESMRRHVI CAPLRRAVI	AZMVINO AZMVAMO AZMVAMO ALVO ALVO ALVO ALVO ALVO ALVO ALVO ALV	TVCSA TLCSA TLCSA AFCSA AFCSA TLCSA TLCSA TLCSA TLCSA TLCSA TLCSA TLCSA TLCSA TVCSA TVCSA TVCSA	TAAGDTC TAIGDAC TAIGDAC TAAGDTC TAAGDTC TAAGDTC TAAGDAC	CGALMLA CGGVMLA CGSVELV CGSVFLV CGGAFLM CGGAFLM CGGVFLV CGGVFLV CGAVFLW	AQVVVVS AQMFIVS GQAFTFR SQLFTTS GQMITFR GQMFSFQ GQLFTFG GQLFTFQ GQLFTFQ GQLFTFQ	POHHTFY PqhHwFY PRRHQTY( PRINETY PRINETY PRRHWTT( PRRHWTT( PRRHWTTY PRRHWTTY PRRHWTTY PRRHWTTY PRRHWTY(	DECNCSIYOGHI DECNCSIYPGRI DECNCSIYPGRI DECNCSIYPGHI DECNCSIYPGHI DECNCSIYTGHI DECNCSIYTGHI DECNCSIYTGHI DECNCSIYPGHV DECNCSIYFGHV DECNCSIYFGHV DECNCSIYTGHV DECNCSIYTGHV	
SEO ID NO: 81-84 85 77-80 86-90 60-76 52-59 91 93-94 95 92 96-101 102	Genotype (IV/2b) (2c) (III/2a) (V/3a) (II/1b) (I/1a) (4a) (4c) (4d) (4b) (5a) (6a)	123 TGI 123 TGI 123 SGI 123 TGI	IRMAWDMMI IRMAWDMMMI	MWSPTT MWSPTa MWSPTA MWSPTA MWSPTL MWSPTT MWSPTT MWSPTT MWSPTA MWSPTA MWSPTS MWSPTS MWSPTT	TMILA TMILA GMVVA ALVVS ALVVA TLLLA TLLLA TLVLA ALIMA ALVMA	YLVRIPE Yamrvpe Hvlrlpç Qllripç Qllripç QIMRVPI QUMRIPS QLMRIPS QILRIPS Qllrips	EVILDIV. EVIIDIII AVIDDIII AVIDDIII AVIDDIII AVIDDIII AVIDDIII AVIDDIII EVIDDIII EVIDDIII EVIDDIII EVIDDIII	IGGHWGVI BGAHWGI AGAHWGV AGAHWGV AGGHWGV AGGHWGV AGGHWGI IGGHWGV AGGHWGV	MFGLAYFS mFGLAYFS LAGLAYYS LAGLAYYS LAGLAYFS LAGLAYFS LVGLAYFS LVGLAYFS LVGLAYFS LVGLAYFS	MQGAWAKVIAI MQGSWAKVIVI MQGAWAKVAII MQGNWAKVIIV MYGNWAKVIIV MQGNWAKVILV MQANWAKVILV MQANWAKVILV MQSNWAKVILV MQSNWAKVILV SAANWAKVILV MAGNWIKVILV	•
J4 - 4U4	Card Cirild	Gi				~ .		J			

## FIGURE 2H

	SEO ID NO:	<u>Genotype</u>		
	81-84	(IV/2b)	184	LLLVAGVDA
	85	(2c)	184	LLLTAGVEA
	77-80	(III/2a)	184	LLLaagvda
	86-90	(V/3a)	184	MvMFSGVDA
~	60-76	(II/1b)	184	mLLFAGVDG
	52-59	(I/1a)	184	LLLFaGVDA
s	91	(4a)	184	LFLFAGVDA
•	93-94	(4c)	184	LFL£AGVDA
	95	(4d)	184	LFLFAGVDA
	92	(4b)	184	LFLFAGVEG
	96-101	(5a)	184	LFLFAGVDa
	102	(6a)	184	LFLFAGVEA
	52-102	consensus		GV

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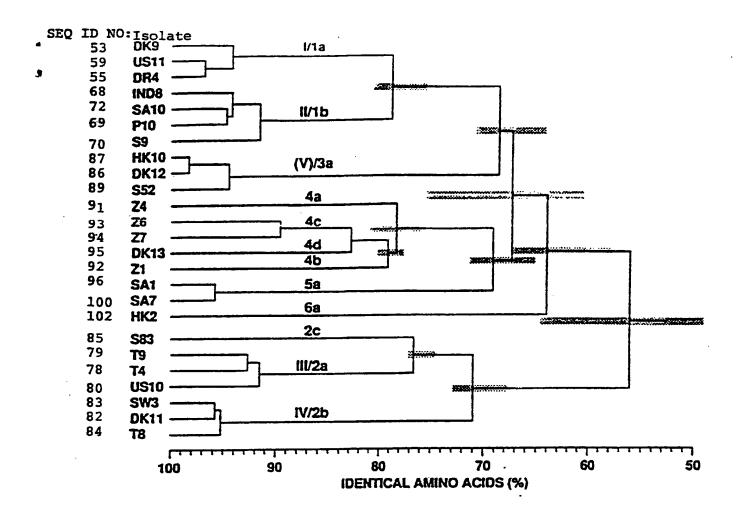
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FIGURE 3

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FIGURE 5

